Transactions of the American Association of Obstetricians,
Gynecologists and Abdominal Surgeons
Sixty-first Annual Meeting
Hot Springs, Va., Sept. 7, 8, and 9, 1950

OUR RESPONSIBILITY

Presidential Address*

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NO distinction, in this country at least, can be greater among members of our specialty than the selection of an individual for the high office with which you have honored me. It is by no means an empty honor, for it carries with it certain responsibilities which must be met with judgment and single devotion to the welfare of the organization. Not the least of these responsibilities is the presentation of what has been known since the beginning as the annual Presidential Address.

Each of my 60 predecessors has splendidly met this obligation. Many of them have utilized it as an expression of philosophies pertinent to the medical aspects of the times in which they worked and wrote. It would seem that such a number of brilliant minds must have encompassed through the years all the thoughts that might be useful in such a presentation and that there is a dearth of material left to talk about. To so large an extent is this true, that it might be possible to plagiarize almost unchanged some of the Presidential Addresses of the past, did one not fear that a few of you might detect the plagiarism.

So I approach this effort of my own with a great deal of trepidation in trying to express adequately my appreciation of your choice of me to lead you even for a brief interlude in the glorious history of the Association. The heartfelt depth of that appreciation cannot be expressed in any words that I can summon to my command.

My address should tell you something of the progress of the Association during this administration. This I will do but very briefly. We have, of

course, mourned the passing of some of our beloved friends. We have, to partly balance our sense of grief in their loss, the contemplation of the splendid Fellows who have joined our membership during this period. Some functional changes there have been in our methods and work, but in putting them into operation they have been handled with so much mutual consideration that the well-being of the Association in the attitude of the Fellows toward its management has, I think, been maintained. The actual clinical work represented by our midyear meeting in Rochester and by the program prepared for this meeting is obviously of a caliber commensurate with the high standards of the past. All of us have contributed to these good accomplishments of the present administration. Of course, I am free to confess that the part of the President in them has been a minor one, and that by far the greatest measure of credit for the smooth functioning of the organization up to the present moment has been due to the devotion and indefatigable work of our Secretary, Dr. LeRoy A. Calkins.

The great doctor has almost always been a teacher. The illustrious physicians whose names have come down to us out of the dim past as outstanding in the general field of medicine and in the specialities, were all teachers. Upon their pre-eminence at teachers largely depends their place in the galaxy of the famous. For our only knowledge of the great among our forebears is their published works which have survived in one form or another, and through various channels, the ravages of the ages. Only one who was in some sense a teacher would leave such imperishable memorials behind him for the evaluation of his eminence by subsequent generations. Out of the many millions of doctors among whom they dwelt and worked, the few thousand whose names constitute the whole list of the "Who's Who in Medicine Throughout All Time," knowledge of whose personality and work has survived to our own and succeeding generations, were all teachers. A medical historian of no mean caliber, says, "The men who loom large were the broadminded, humanely sympathetic, deeply educated physicians, who treated men in their ills rather than their ills without due consideration of the individual, and not only relieved the discomfort of their patients and greatly lessened suffering, and added to the sum of human happiness in their time, but also left precious deeply significant lessons for succeeding generations of their profession." I am sure that each one of us might wish to "loom large" according to the precise definition here outlined.

So one would suppose that as such teachers have existed at almost all times during the history of human experience, their teachings would form a constantly accumulating body, accessible to all their followers and making a consistently more valuable summation of medical knowledge for publication to all doctors, on a steadily improving, constantly higher plane as time went on.

That has not however been true in any field of human achievement and knowledge. Secrets possessed by the ancients in metallurgy, in engineering. in weaving, in the manufacture of pottery and in many other fields of human ingenuity and achievement have been lost and never recovered. The same

thing is eminently true of medicine. The whole history of medicine indicates that men of all times have faced their problems, which were very much those of our own time, in almost precisely the same spirit as we do ours at present. Their solutions of them were always interesting, often adequate and more frequently than we would like to think possible, resemble our own in many ways. But these results of their thought and ingenuity have time after time been lost sight of, making it necessary for men of future generations to repeat their thought, copy their ingenuity and capacity, and achieve all over again what had been done long, long before.

Even under the favorable conditions for the dissemination of knowledge which we believe characterize our own era, minor instances of achievement being forgotten and reborn are not lacking. Rucker has stated that the operation attributed to Dührssen under the name of "Dührssen's incisions" was actually performed by a country surgeon of Virginia before the date of Dührssen's birth. I recently heard Rudolph Holmes, in an informal talk, state that the bone plates and the intestinal anastomosis button for which the late Drs. Senn and Murphy, respectively, bear current credit, were both envisaged in principle, and used, many years before those gentlemen devised them. A supravesical extraperitoneal cesarean section was conceived about a century and a half ago and attempted and actually carried out more than a third of a century ago. Thus, without derogation of Waters for having developed it into an intensely practical addition to our present-day surgical armamentarium, it may be recognized that his brain in undertaking it, was but following in the tracks of other brains long antedating his work. Such detailed instances of work developed, completely dying out of the ken of succeeding men, and again being rediscovered by still other men could doubtless be multiplied throughout medical history.

This waxing and waning of medical attainment through the centuries can be roughly graphed almost like a fever chart. Primitive medicine, of course, had its genesis with the beginnings of man's existence in all localities and in some localities within the period of recorded history had attained some degree of proficiency. This development is well known in relation to the early Egyptians, the great Sumerian nations, the ancient Jews, and the nations of the Orient as far east as Japan. Early Greece, of course, shared in this type of medical development. None of these phases would however show at a very high point in the graph. But by about 460 B.C., for a period of 300 years more or less, the combined influences of all of these early developments reached a high culmination in what is referred to as the classic period of Greek medicine. From this high point of medical development in the ancient world to the fall of the Roman Empire, the great influence of Greek medicine was felt strongly in all parts of Europe and the Middle East, as in Rome, Alexandria, the Byzantium, the far-flung Mohammedan Empire, and Western and Central Europe.

All of this influence, however, showed a general deterioration from the high point of the Greek classic period, so that at the time of the fall of the Roman Empire about A.D. 476 medicine throughout Europe had sunk to a low

ebb. During the middle ages, from the fall of the Roman Empire to about the middle of the fifteenth century, most people consider that there was no real progress in medicine in Europe. All, however, do not share this belief. One historian points out that "our medieval medical colleagues faced the problems of medicine and surgery that are now interesting us, in very much the same temper of mind as we do, and very often anticipated our solutions of them . . . the medieval generation actually did much more than is usually thought." During the first half of the period from the fall of the Roman Empire to the end of the fifteenth century, there was a marked decadence of all intellectual life, because the barbarians who were responsible for the fall of that Empire had no heritage of culture, no interest in the intellectual life, no traditions of science. But in the latter half of this medieval period there was a resurgence of no mean order and it was during this period that many of the early important schools of medicine, beginning with that at Salerno, in the tenth century, were founded. The beginning of this resurgence in southern Italy was stimulated by the strong Greek influence which had from much earlier times predominated in that part of the peninsula. Especially in surgery did this period of the late middle ages show remarkable development.

The latter part of the fifteenth century, embracing as it did the all-important invention of printing and the impetus given to all learning by the discovery of America and of other wide-flung lands all around the globe, witnessed the effulgence of the Renaissance. During the seventeenth and eighteenth centuries, however, there was somewhat of a backsliding and decadence in the general progress of medicine in spite of much that was admirable, and of many high individual bright spots.

Modern medicine, while far antedating the nineteenth century in its beginning, has had its most glorious flowering in the nineteenth and twentieth centuries. Now, in the middle of the twentieth century, we pride ourselves on an advancement which the world has never heretofore seen. We proudly point to anesthesia, to antisepsis, to asepsis, to the fine development of the basic sciences, pathology, physiology, biochemistry, and very recently tremendous broadening of the horizon of therapeutic resource other than surgical. Furthermore, we note with satisfaction that numerous publications, together with the shrinking of the world, and ease of intercourse between races of men, by reason of improvement in communication of all sorts, have made all of these achievements, as fast as they have developed, the common property of mankind.

It is not unimaginable, however, that this feeling of complacency was shared by the physicians of other periods of brilliant medical achievement. The Greeks may very well have possessed it. We know that the great Ambroïse Paré felt it so strongly that he wrote, in effect, that surgery had come to such perfection in his own hands that it was hardly to be believed that future generations could add to or improve upon his attainments.

Indeed the American Medical Association in a communication as recent as March 7, 1950, states, "Medical education was at a low ebb less than fifty years ago," and continues to refer to the "present high level" of medical

education. Yet I am sure that each one of us who knows anything about the present widespread discussion and criticism of every phase of our under-graduate and postgraduate medical education will agree that the "high level" referred to falls far short of the ideal. Our own complacency may prove in the light of history to be fallacious.

So, standing upon this peak, it may be well to ask ourselves, where we are going from here? Will there be a continuing increase in the achievements of medicine, as we confidently hope and expect, or will there be again a de-cadence from the high point to which we in our pride think we have risen? To quote Walsh, "It does not seem possible that mankind should ever lose sight of the progress of medicine and surgery that has been made in recent years, yet the history of the past would seem to indicate that, in spite of its unlikelihood, it might well come about."
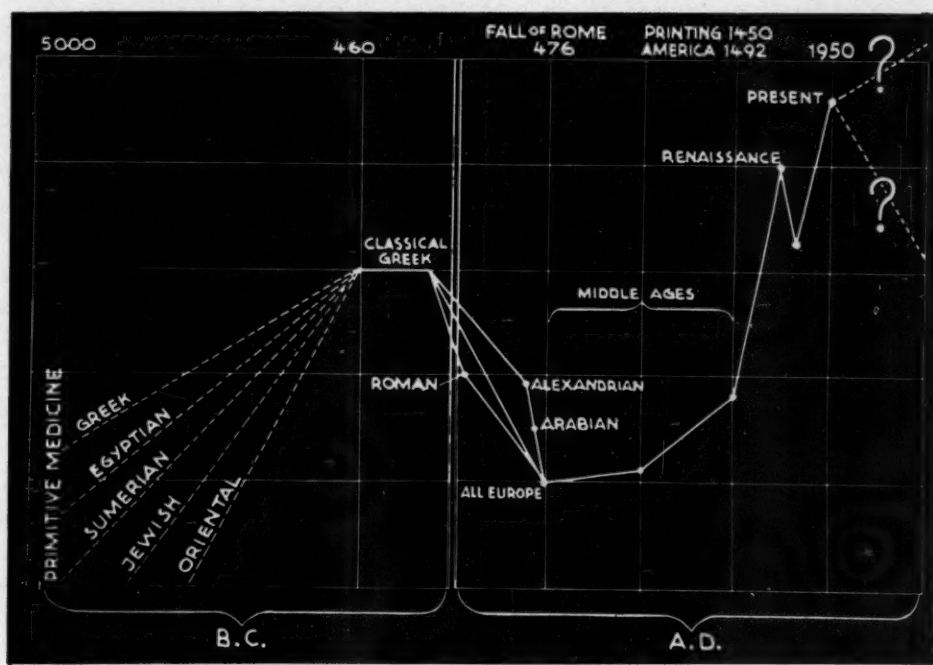
Fig. 1.

Why are this thought and this question brought to your attention at this time? A comparison of the rise and fall of medical culture which I have at-tempted to sketch to you, in parallel with all culture, and the waxing and waning of the political and economic histories of nations, indicates that broadly one depends very pertinently on the other. In other words, as each civilization in turn has reached the zenith of its political and economic power, its particular culture has also reached its zenith, while cultural decay follows the decay of the civilization in its political and economic status. We, today, in our political and economic power, are stronger than any other national civilization has been before us. But the civilization of the whole world is as unstable as it has ever been in recorded history. Within the lifetime of

even the youngest of us, the last great world dominion has been shattered. The European cradle of many civilizations is in a chaotic state necessitating the utmost struggle to salvage what remains of the last vestiges of those civilizations. The great stronghold of conservatism, Britain, has been for some years dominated by the very antithesis of conservative economic concepts. Our own vaunted economic and industrial being is, I am afraid, less secure than it has been at any period since the Civil War, and what the end may be no man can tell. Medicine itself has been nationalized on the continent of Europe, in Great Britain, in the Antipodes, and to a larger extent than we would like to acknowledge, amongst us. Not improbably, if not inevitably, this may become complete as it has among our British cousins. Indeed, if the fears of some scientists or pseudo-scientists are well founded, the entire civilization of our globe may succumb to recently developed sources of destruction which will force man, if he survives at all, to rebuild civilization from the same beginning whence he started aeons ago. Hence there is a chance, as envisaged I think by all of us, that medicine will deteriorate in many regards, as the economic and political characteristics of our country may change.

Those of us who fear this deterioration believe that it will affect most seriously the intangible but highly important phases which we believe most significantly characterize our present high attainment. Among the more important of these intangibles is the recognition of the responsibility of each of us to teach those who come after us not only the material things of medicine, but the great ideals which constitute the throbbing heart of medicine, the ideals of self-sacrifice, of service over and beyond pecuniary gain, the development of medical and social conscience, and its application to every phase of our work.

Medicine from the very earliest times has been the handmaiden and close companion of religion. Primitive medicine in all times and in all places was practiced by the religious leaders of the peoples. Aesculapius, the great prototype of all physicians in the prehistoric Greek era, was actually said to be the son of the god Apollo, physician to all the Olympian gods, by the nymph Coronis. He was taught by the Centaur Chiron, son of Saturn. He was destroyed because Pluto, the god of the underworld, accused him of being so proficient in his medical attainment as to seriously affect the increase in growth of the inhabitants of the hell over which Pluto reigned. So that Aesculapius as the years went on became identified not only as the father of Hellenic medicine but an actual god. Close affiliation between medicine and representatives of religion has continued through all the ages since. Monastic scholars during the medieval period preserved for the world the great treasures of the ancient manuscripts of Greece and subsequent civilizations. In all times in primitive countries the doctor and the priest were often combined in one person. That is true of the colonial periods of our own history. The first great physician of New Jersey was a Presbyterian minister. Cotton Mather, the great divine of the early days in Massachusetts, was a physician of sorts. His contemporary, Thomas Thatcher was "equally re-

nowned as preacher and physician.'' Similar individuals in Virginia and in the far-reaching expansion of our eastern seaboard civilization to the westward were not infrequent. For centuries, all over the world, to the present, the devoted medical missionaries of all Christian faiths have splendidly exemplified the same dual function. Even today there is an inchoate impression in the minds of many of the laity that the priest and the physician have something of a common function. Nothing warms me quite so much as to have an earnest patient in the midst of a confidential appeal for help in her extremity of mind and body, inadvertently but nonetheless sincerely call me ''Father.'' This identity of physician and priest in their common objectives is necessarily an outgrowth of their so similar functions. Both are engaged in the very direct service of the Almighty and of mankind. Both are imbued by ethical and sacrificial motivation which is closely akin. Perhaps one prays just as earnestly as the other for God's blessing on his work of service. Woe to medicine when physicians forget that their work, like that of the priest, is to God and to God's creatures.

If these changes which appear so imminent and so disastrous eventuate in whole or in part, every one of us is going to be affected by them in some manner and in some degree. Some of us will ourselves be forced to a deterioration of practice most subversive of those ideals to which we have long been devoted, and most discouraging physically and psychically, as has been exemplified in the experiences of many of our British associates. These undesirable effects may very well be most disastrously felt by the great body of general practitioners throughout our land.

I am not qualified as an economist, nor as a politician, medical or otherwise, to discuss the means of averting the broad changes alluded to. Nor do I believe that our own group, except as its members individually function as integers in other groups, has a direct responsibility in relation thereto.

But one direct responsibility we do have. Our corporate being has for its *single* objective, as quoted from our Constitution, ''the cultivation and promotion of knowledge in whatever relates to obstetrics, gynecology and abdominal surgery. . . .'' In other words, the sole object of our Association is to teach.

If we specialists and teachers actually feel the effects of possible changes in medicine in less degree than some of our fellows, it is the more incumbent on us to exercise assiduously the glorious privilege of passing on to those who surround and depend upon us, as well as to those who shall follow us in the years to come, all the lessons of history, of personal experience, of observation, of adroitness, of attainment, which we possess. This to the end that in spite of environmental pressures the attainments of medicine shall not grow less, but shall proceed to develop to an even more glorious future. Let us then, in the presence of malign threats which none of us can measure, solemnly rededicate ourselves to the obligation which we have inherited from those who taught us and continue, no matter what our individual circumstances are, to ''gladly teach.''

THE DANGEROUS PLACENTA*

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"My Colleagues will be my Brothers."

THESE words are found in the Declaration of Geneva adopted by the General Assembly of the World Medical Association in September, 1948. Wherever there is freedom of thought, and of living, this grand concept of medicine applies, and has applied from earliest times. Leaders of the Profession in the Old World and the New have shared their knowledge and inspiration with men and women of all races and colours. Such a leader was Dr. Joseph Price in whose memory this Oration was founded. I am indeed grateful for the honour of being invited to join the ranks of those who from across the Atlantic have year by year paid tribute to a great American surgeon, one of the founders of this Association, and one of its early Presidents. Dr. Price was a surgical pioneer of outstanding courage and ability, as revealed by the amazing results achieved early in his career in the treatment of peritonitis by abdominal drainage. It is recalled that the first occasion on which, as a young man, he performed this operation, was on a woman allegedly dead from the sepsis of a criminal abortion. Her recovery almost recalls the Biblical story of the raising of Lazarus. This was the beginning of original work of the greatest merit in abdominal and vaginal surgery. It is of some satisfaction to a visitor from England to recall that early in his experience Dr. Price came under the influence of Mr. Lawson Tait of Birmingham, whose clinic he visited on several occasions. Dr. Price regarded Mr. Tait as his idol and master, and was acknowledged by him as his most distinguished American visitor. Just as Dr. Price made opportunities of visiting Lawson Tait so, as his own prowess as a surgeon and teacher became more widely recognised, he attracted to his clinics a constant flow of colleagues anxious to learn his methods. Among other tributes paid to his surgical skill, his brilliance in discussion, his charity and kindness, Dr. Howard Kelly maintained that Dr. Price had taught more men Gynaecology, (and better Gynaecology) than any man in America.

"I will give to my Teachers the Gratitude and Respect which is their due."

So reads another promise in the Geneva Declaration. In paying this brief and inadequate tribute to a great American surgeon, may I also record appreciation of the generosity and vision of his distinguished junior colleague and pupil, Dr. Kennedy, by whom this memorial Oration was endowed as a lasting tribute to his great chief and teacher.

I realise, Gentlemen, that this is an Association of practical men, and that the man whose memory we honour this evening was distinguished in his day

and generation because of his forthright and practical approach to the problems which faced him. For that reason I have chosen a clinical subject, which I hope will commend itself to you. It deals with one aspect of haemorrhage in obstetrics, responsible for some of the more dramatic incidents of our professional lives, and fraught on occasions with grave danger to both mother and child. The title chosen is "The Dangerous Placenta," a title which may well be criticised for, after all, what placenta is not dangerous? It may be too small (or degenerate excessively) and result in the death of the foetus in utero; it may separate prematurely with dire results; it may erode and weaken uterine scars and provoke rupture and maternal death; it may be normal in every respect, but give rise to postpartum haemorrhage as a protest against mishandling of the third stage of labour; or, as known since the days of Hippocrates, and probably long before, it may be the cause of antepartum haemorrhage of varying severity. It is my purpose to consider some aspects of the last group. My subject deals with the low-lying placenta, and particularly with the one attached to the posterior wall of the uterus. It is this posterior placenta praevia which I have described as "The Dangerous Placenta."

My attention was focused on it by a tragedy on the Eve of Christmas, 1940. A primigravida of 30, with no history of bleeding, was admitted at term from the antenatal clinic because of a high and unstable head. The provisional diagnosis on the admission sheet was placenta praevia. At the thirty-sixth week the pelvis had been assessed as being of adequate size and shape. Early on the morning following admission, labour commenced spontaneously with rupture of the membranes, a bright loss, and fair pains. Because the bleeding supported the provisional diagnosis of placenta praevia the patient was examined in the theatre. The head was at the brim but not engaged. The cervix was two fingers dilated, the forewaters were ruptured, and the placenta was posterior but not reaching the internal os. It was decided to allow labour to continue. Blood was prepared but not given, and the usual precautions were taken to see that any haemorrhage would be reported at once.

In England in 1940 this placenta was described as lateral; to-day it would probably be classified as belonging to Type 1 or 2, while in America I imagine it would be regarded as a "low-lying placenta" by those who accept the classification agreed upon by several of your eminent authorities, Greenhill, Titus, McCormick, and Eastman. The decision to allow vaginal delivery with this type of placenta was in keeping with our usual practice at that time. Indeed, if one is to accept the teaching of even the latest editions of many textbooks from both sides of the Atlantic, the treatment to which I refer, and on which I will comment from time to time this evening, is still taught and practised in many centres.

Pains were ineffective and although bleeding was slight the general condition of the patient deteriorated and nine hours later, with the head still free, I performed caesarean section. When the child was delivered it was found that although the placenta was high on the posterior wall of the lower

segment, as detected during the vaginal examination, it nonetheless was sufficiently low to be lying over the promontory of the sacrum. It displaced the head forward and prevented it from engaging. Surprisingly little bleeding occurred during the operation, but as previously recorded the patient's condition was not good and a transfusion was commenced when she was still anaesthetised. Shortly after waking from the anaesthetic the unfortunate woman collapsed and died. To complete the tragedy the apparently healthy baby died 24 hours later and was found to have a congenitally deformed heart. This happened nearly ten years ago, and in retrospect there is much to criticise in the way the case was handled. Particularly so when at autopsy it was found that an underlying primary anaemia had not been detected clinically. Failure to appreciate this was undoubtedly a main contributory factor in causing the fatal collapse during transfusion.

The tragedy taught us much, and in the years since then we have made in the Area Department at Oxford a particular study of placenta praevia. One result has been that from that day until this was written, there have been no maternal deaths from haemorrhage either within the department, or on the emergency flying squad service which, based on the Radcliffe Infirmary at Oxford, answers calls over a wide area of five counties from midwives and doctors in difficulty. This emergency service which is the joint responsibility of the Nuffield Department of Obstetrics, under Professor Chassar Moir, and the Area Department for which I am responsible, has answered over 300 emergency calls of which nearly 90 per cent were for postpartum haemorrhage. Five of the women treated by my Department were suffering from antepartum haemorrhage and had bled seriously from major degrees of placenta praevia. The condition of three was so critical that as they were 25, 40, and 40 miles, respectively, from Oxford, the necessary team was taken to deliver them in the cottage hospitals to which they had been admitted by their own doctors. These three patients, and the two others who, after transfusion, were brought into the Radcliffe Infirmary are included in the series now to be reviewed.

In the nine and a half years since the tragedy to which I have referred 245 women have been treated for placenta praevia in my department. This represents approximately 40 per cent of all those admitted with antepartum haemorrhage. The percentage is high because many of those whose bleeding was due to cervical causes were diagnosed and treated in the outpatient department, not admitted, and therefore not included in the series. Others whose bleeding was not from the cervix were not admitted when it was considered clinically and radiologically that a placenta praevia was not responsible. The method of assessing these factors will be described later. The exclusion of these cases is the main reason for the relatively high incidence of placenta praevia in this group.

These have been years in which two of the major causes of maternal mortality, haemorrhage and sepsis, have been dramatically and successfully attacked throughout the world by the increasing use of safer blood transfusion, antibiotics, and chemotherapeutic agents. Only eleven years ago an article

published from Oxford making a plea for the wider use of blood transfusion in obstetrics started a prolonged controversy in the *British Medical Journal.* One or two of the senior and most distinguished obstetricians of the British Isles were among those who attacked the article as advocating a dangerous innovation likely to lose more lives than it saved. Today, with due recognition of its immediate and remote dangers, blood transfusion has taken its place in the vanguard of life-saving measures. During the same years, progressive discoveries in the field of chemotherapy have resulted in countless lives being saved. A glance at Table I will show how, in the treatment of placenta praevia, the maternal and foetal prognosis has improved during the last fifteen to twenty years. These results must be kept in perspective, however, for they were achieved in large hospitals and teaching units, and under less favourable conditions the mortality figures would be much higher. That there is still a problem to be solved in the treatment of placenta praevia is known to us all, and is illustrated as far as England and Wales are concerned by the fact that 247 mothers were registered as dying from placenta praevia in the five years ending 1948. These figures, provided by the Registrar General, must be regarded as optimistic, for it is certain that at least some deaths due to placenta praevia will be certified as due to other causes and not included here. Nonetheless, it is apparent that the results have progressively improved, and our problem now is to consider how they may be made even better. I believe they can, and in the following ways: (1) by early diagnosis; (2) by improved methods of treatment; (3) by a better selection of cases for the treatment available.

TABLE I. PLACENTA PRAEVIA

AUTHORITY	YEAR	TOTAL CASES	MATERNAL MORTALITY	FOETAL MORTALITY
D. Findley	1921	15062	6-7.8%	26-58%
	1922-37	32766	5.9-6.4%	24-57%
Sir Comyns Berkeley	1936	4580	7%	59%
New York Lying-In	1932-43	155	0.6%	25%
F. J. Browne	1944	3103	5.9%	54%
Manchester Glasgow Rotunda	1941-45	835	3%	36.4%
Belfast (Macafee)	1937-45	191	0.5%	22%
Oxford (Present series)	1940-49	245	0.4%	18%

The series from which our experience has been gained, and on which the following comments are based, is not a vast one when compared with the statistical surveys of Findley, Berkeley, or Browne, but it has the advantage that all the patients were treated by one team in which ideas and experiences were shared. It includes in all only 245 cases, and to avoid any criticism of bias this number has been further reduced for detailed analysis to 170 by the exclusion of no fewer than 75 cases of antepartum haemorrhage indexed as due to placenta praevia. Patients included in the series consist of those in whom the placenta was seen or felt in the lower segment by a senior member of the department, while those rejected consist of patients who, for varying reasons, were not submitted to vaginal examination by such a member. They

are rejected in spite of the fact that in some the placenta had been felt by a resident doctor, while in others the praevia position had been confirmed radiologically, but the point common to all in the group was that *the presenting part was in the pelvis when the patient was seen by a senior obstetrician, and bleeding had ceased.* For this reason a further vaginal examination was considered unnecessary. The importance of the fact that in this group the presenting part was in the pelvis will be emphasized later.

It may well be argued that there is no need to exclude these cases from the series, but their exclusion or inclusion is irrelevant to the final deductions, and we have erred on the side of being overcritical in our analysis lest criticism of the selection of material should detract from the importance of the conclusions. For the same reason, in the subsequent presentation of results, no attempt has been made to give these in any corrected form. The figures, maternal and foetal, are those actually obtained, and whatever the cause of death it is from the point of view of this discussion included as due to placenta praevia. It is certain that some of you would agree that in doing so we have been almost unfairly severe, but it is equally certain that with this background we are in a position to assess the true value of the methods advocated and results obtained.

1. Early Diagnosis

This is important for two reasons. It enables the patient to be placed under favourable conditions for dealing with an emergency before this emergency arises. The result is that in many cases the placenta praevia can be dealt with as an elective procedure with minimal risk to the mother and child. All that is required to achieve this early diagnosis is the correct attitude of mind on the part of the doctor in the antenatal clinic, for there is nothing new in the idea that a high head or malpresentation may be due to placenta praevia. This answer can often be obtained from a medical student, but it is all too seldom put into practical effect and made the reason for the further investigation of an antenatal patient before the thirty-sixth week, unless here is also the story of some vaginal bleeding. In the series of 170 under review 20 had an oblique or transverse lie on admission, 15 had a breech presentation, and 20 had a vertex so high and unstable that a note was made to this effect on the admission slip. There were in all 35 malpresentations of major degree, an incidence of 20 per cent. It is interesting to note that 28 patients, or 16.5 per cent of the series, *were admitted before any haemorrhage occurred.* The attitude of mind in the antenatal clinic to which reference has been made is responsible for this, and is one to encourage. The percentage admitted before bleeding should be even higher.

It may appear at first sight that this procedure would cause administrative difficulties because of the needlessly early admission of many patients with high heads or unstable presentations due to causes more innocent than placenta praevia. The reason why this need not occur leads to the second aspect of the problem of early diagnosis.

In many, if not most of the world clinics, it is still believed that the only way to diagnose a placenta praevia is to feel it. For the reasons already given this criterion has even been accepted in collecting the series under review, but before any vaginal examination was made a placenta praevia was diagnosed radiologically in 48, that is, 28 per cent of these patients. It is our opinion that improved radiological methods of placental diagnosis constitute one of the major advances of obstetric practice. This figure of 28 per cent requires a little more consideration. It does not indicate the percentage accuracy of the new technique. We believe this is nearly 100 per cent, and experience of it in the last few years supports this belief. In many emergency admissions due to antepartum haemorrhage the clinical position is such that no radiological assistance is required. The maximum value of the radiological method is that it permits of a preliminary selection from those cases suspected in the antenatal clinic of having a placenta praevia. A decision whether admission is necessary can often be made on the radiological support or opposition to the provisional clinical diagnosis. A further important practical application of the new technique is that it enables a diagnosis of the cause to be made in patients who have been admitted with bleeding when this is not of such severity as to demand immediate clinical investigation and treatment. In most hospital series placenta praevia is the cause in less than 50 per cent of those patients admitted with antepartum haemorrhage, but the decision on whether it is responsible or not, is one of major importance to both the mother and her baby. It is now possible to determine those in which it is responsible, without the necessity of a vaginal examination and its attendant risks of inducing premature labour. In this way it is no longer necessary to keep patients with antepartum bleeding but without a placenta praevia in hospital, maybe for weeks, if one is adopting the expectant attitude advocated and practised with such excellent results on both sides of the Atlantic by Johnson, Macafee, and others. Radiology is a valuable aid in the selection of cases suitable for this treatment.

The pioneer work on soft tissue radiography in placental diagnosis was conducted in America, and the names of Snow and Powell (1934), and Dippel and Brown (1940), to mention but four, at once come to mind. All are familiar with the controversy their work produced in respect of the claims made on its behalf. At a time when from a purely clinical aspect we were becoming progressively more interested in the early diagnosis of placenta praevia, we had the good fortune to have associated with us Dr. F. Reid of the Department of Radiology at Oxford. Dr. Reid was developing a technique of his own of soft tissue placentography without the use of contrast media. This technique has been fully described in the *British Journal of Radiology* of October and November, 1949, and I will do no more than mention two of its basic principles. The first is that by using a wedge-shaped aluminum filter a much better definition of the whole field is obtained with the long exposure necessary in taking films of the abdomen and pelvis in the later weeks of pregnancy. The second principle is that the effect of gravity can be used by suit-

ably posturing the patient in the erect and semierect position, and in this way not only is the presence of an obstacle preventing engagement of the presenting part detected, but its exact relation to the pelvic brim is defined. Many of the points illustrated radiologically should of course be detected first clinically. For example lateral, forward, or upward displacement of the presenting part can be assessed by abdominal palpation. Other details would require vaginal examination for their detection, and it is by avoiding the necessity of this when the foetus is premature that the x-ray technique makes its biggest contribution. It will be seen that the radiologist can assist in one of two ways; he may demonstrate the placenta itself, or failing this he may infer its presence by demonstrating a soft tissue cause for the foetal displacement. The more experienced he becomes the more often he will outline the placenta and define the exact limits of its attachment.
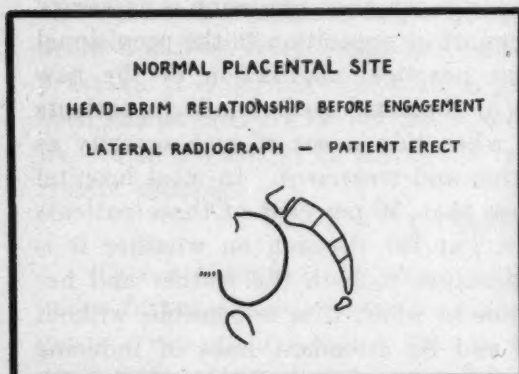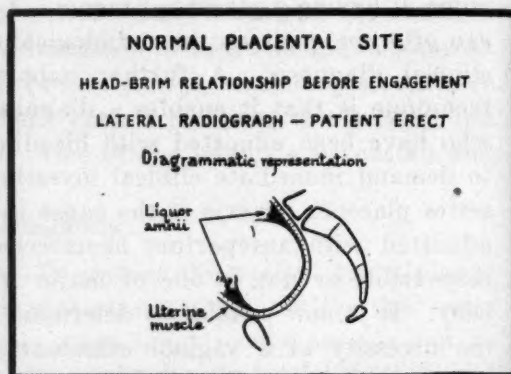

Fig. 1.

Fig. 2.

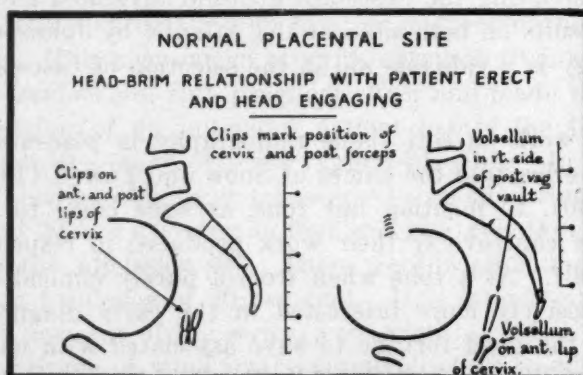
Fig. 3.

The preceding illustrations which are scale drawings of actual films made from patients in this series, demonstrate these points. Fig. 1 portrays the normal head-brim relationship before engagement of the head when the patient is erect. Fig. 2 is a diagrammatic representation of the same pelvis to show the soft tissue relationship. The next illustration (Fig. 3) is of interest because

it indicates the relative positions of the anterior and posterior lips of the cervix, the posterior vaginal vault, and the promontory of the sacrum, when the head is engaging in the brim. This diagram was drawn to scale from lateral films taken to demonstrate the position of clips attached to the lips of cervix, and the posterior vaginal vault, before labour commenced in a primigravira with a normal head-brim relationship in which the presenting part engaged when the patient was erect. The main point to which attention is drawn is the distance from the external os to the promontory of the sacrum which, in this film, measured approximately 10 cm. Reid analysed 15 films from a random series of lateral radiographs and found the mean figure of 7.1 cm. for this distance from the cervix to the promontory. If it is accepted that the junction of upper and lower segments in the last few weeks is approximately at the level of the pelvic
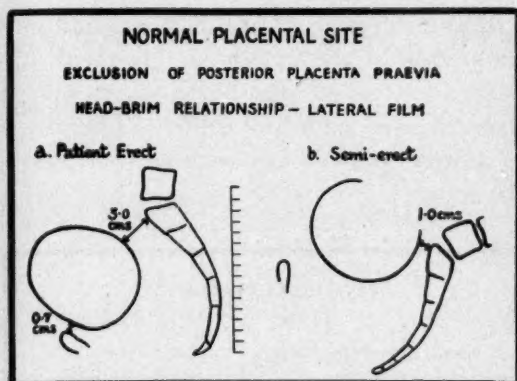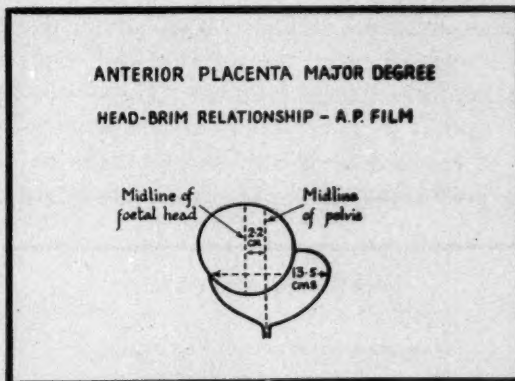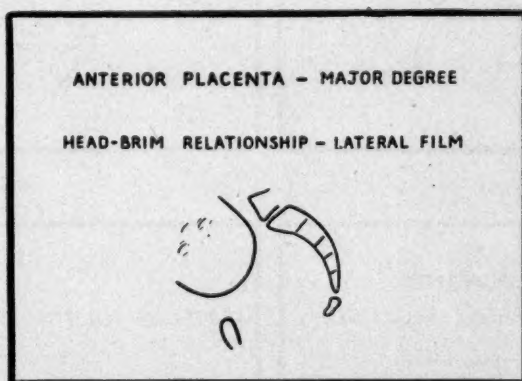

Fig. 4.

Fig. 5.

Fig. 6.

brim, as described by Marshall (1939) it will be realized that a placenta attached to the lower segment may still be 7-10 cm. away from the examining finger as it passes through the external os. It would be classified as merely a Type 1, or low-lying placenta. The practical significance of this will be emphasised later.

Figs. 4, 5, and 6, which, like the preceding ones, are drawn to scale from actual films, portray some of the disturbances of head-brim relationship for which placenta praevia can be responsible. Fig. 4 demonstrates the effect of gravity on the unengaged head. With the patient erect there was a space of 3 cm. between the head and the promontory, but in the semierect position this was reduced to the normal of approximately 1 cm. Figs. 5 and 6 show displacement due to a major degree of anterior placenta praevia extending round the left side of the lower segment. This patient had a breech presentation at the 36th week, and when version was performed the head was not only high, but displaced into the right iliac fossa. There had been no bleeding. The anteroposterior films with the patient semierect (Fig. 5) showed lateral displacement of the head 2.2 cm. from the midline, and Fig. 6 demonstrates the head displaced 2.4 cm. back from the posterior surface of the pubis. The radiological diagnosis was "major degree of anterior placenta praevia extending down to cover the internal os," and examination of the patient in the theatre confirmed these findings. There was, in fact, a central or total placenta praevia, and as in many others in this series the diagnosis was made and confirmed before there had been any haemorrhage at all. Lower segment cesarean section was performed and a healthy female infant delivered.
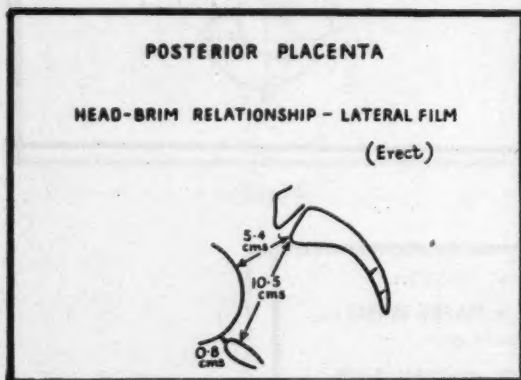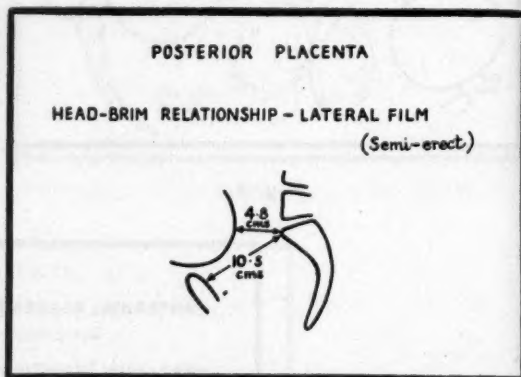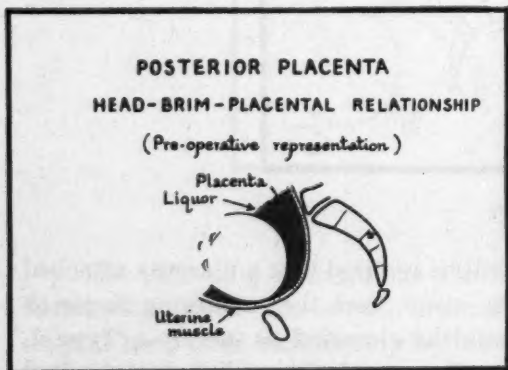

Fig. 7.
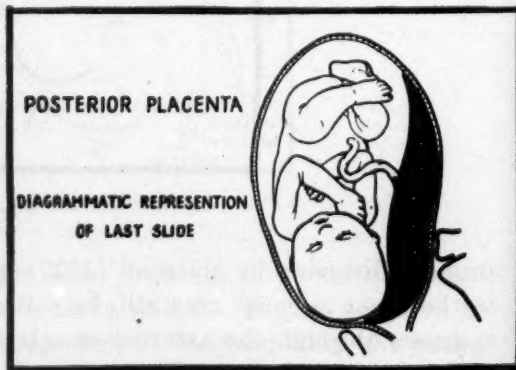

Fig. 8.

Fig. 9.

Fig. 10.

The posterior placenta praevia is even easier to suspect clinically, because as it lies over the promontory of the sacrum it projects the presenting part forward, giving a picture of apparent or real disproportion. This is well demonstrated in Figs. 7, 8, 9, and 10. From these it is seen that in this case almost one-half of the internal conjugate was occupied by the lower pole of the placenta which, contrary to what is sometimes taught in the textbooks, was not thin and easily compressed. In fact, from our studies of this particular point we are not convinced that a placenta praevia is more prone than a normally situated one to these changes in shape. Further evidence on the relationship of the placenta to the conjugate is supplied by Figs. 11 and 12. The first was obtained by injecting Pyelosil into the amniotic sac during cesarean section for a posterior placenta praevia. The lower segment had been exposed, but not opened. The head was pressed into the brim as far as it would go and a lateral picture was taken. Fig. 11 is a scale drawing of the film obtained. The opaque liquor

POSTERIOR PLACENTA

AMNIOGRAPH WITH PYELOSIL

Ant. uterine wall
Opaque Liquor
Opaque Liquor
Negative shadow due to placenta

Fig. 11.

POSTERIOR PLACENTA

LEAD MARKER ON PLACENTAL SURFACE
PLACENTA CONGESTED IN SITU

Fig. 12.

POSTERIOR PLACENTA

PLACENTA INJECTED IN SITU —
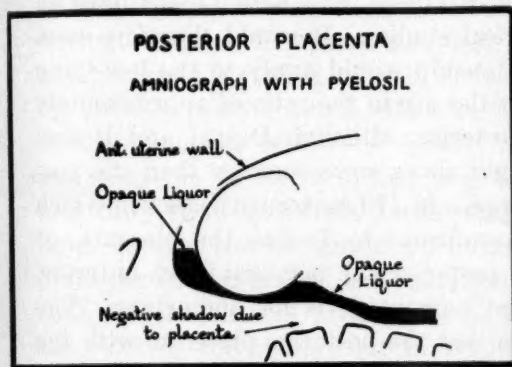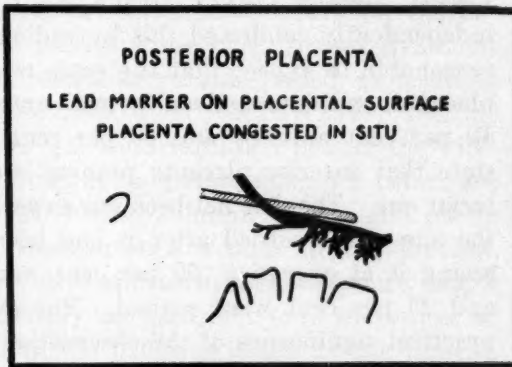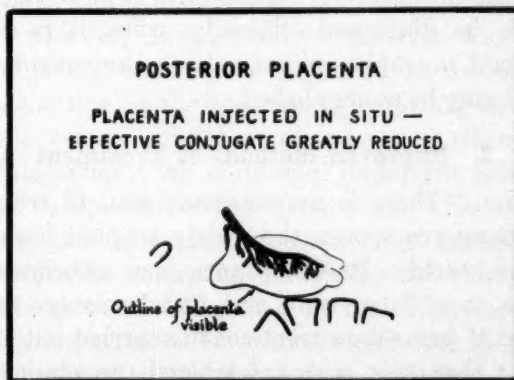EFFECTIVE CONJUGATE GREATLY REDUCED

Outline of placenta visible

Fig. 13.

outlines the surface of the placenta which is seen to be lying over the sacral promontory and displacing the head forward. When the infant was delivered a lead marker was immediately placed on the placental surface, and a further film taken after Pyelosil had been injected into the cord. The result is seen

in Fig. 12 and one point should be noticed. The lower pole of the placenta could just be tipped by the examining finger on vaginal examination. It was not a total placenta praevia, nor even a partial one by the American classification. It was merely low-lying, and in Great Britain would be described as Type 1 or possibly Type 2. Nonetheless, because of its thickness and position in relation to the promontory, and hence to the internal conjugate, it effectively prevented engagement of the head and was therefore a dangerous placenta, dangerous to both mother and babe. An even better picture obtained in the same way and on another patient is seen in Fig. 13. It will be observed in both of these that the cord is attached to the lower pole of the placenta and the risk this entails to the foetus will be apparent, but will be mentioned again later.

One interesting point arises at this stage of the discussion. As one would expect, the normally situated placenta is found with approximately equal frequency on the anterior and posterior walls of the uterus. Dippel and Brown (1940), Stander (1942), Torpin and Holmes (1943), and Reid (1949) have all independently confirmed this by radiological studies. It would therefore seem reasonable to expect that the same relationship would apply to the low-lying placenta, and figures given by most authorities are in the ratio of approximately 40 per cent anterior and 60 per cent posterior, although Dippel and Brown state that anterior placenta praevia is eight times more common than the posterior one. This has not been our experience. In 170 consecutive cases in which the site was recorded after it had been confirmed by feeling the placenta, or seeing it at operation, 50 per cent were posterior, 21 per cent were anterior, and 29 per cent were central. The exact percentage is not important. The practical significance of the observation is that the posterior placenta, with the peculiar problems it presents, is the type most frequently found in a clinical series. Reconciliation of the clinical and radiological findings merely serves to emphasize the point that a low-lying placenta is more likely to cause trouble, and for that reason be diagnosed clinically, when it is situated posteriorly. Sufficient has been said to emphasise not only the importance of early diagnosis, but ways by which it may be accomplished.

2. Improved Methods of Treatment

Jaggard's dictum, "There is no expectant plan of treatment for placenta praevia," has for many years been the widely acepted basis of therapy in the major clinics of the world. Its acceptance was associated with a maternal mortality of not less than 5 per cent, and foetal wastage of over 50 per cent. It is true to say that if immediate treatment is carried out the maternal results should now be better than this, with safer blood transfusion and careful selection of cases for cesarean section, but foetal wastage would remain high.

The truth of the dictum has been successfully challenged by Johnson (1945 and 1950), Macafee (1945, 1946, and 1950) and others. Their brilliant results are based on the fact that prematurity is the greatest cause of foetal death in placenta praevia. They have shown conclusively that in many cases of antepartum bleeding due to placenta praevia, it is possible, when the foetus is pre-

mature, to adopt an expectant attitude until the thirty-sixth or thirty-eighth week without increasing the maternal risks. Essential safeguards are that the patient should be in a hospital equipped to deal with the emergency of haemorrhage. Anaemia is treated on admission, by blood transfusion if necessary, and suitable blood of Rh compatibility is constantly available. Isolation in a single room is best avoided so that there is always someone at hand should bleeding occur. An effective bell should be within constant reach of the patient. Much has been said and written of the advantage to the foetus of this expectant attitude and the evidence is overwhelming. The prognosis for the foetus undoubtedly depends on avoiding prematurity, in spite of the contrary views expressed by Stirling and Tennent of Glasgow (1947). In fact, in no branch of obstetrics has there been such a dramatic reduction in foetal mortality as in the expectant treatment of placenta praevia.

There has been a general tendency to adopt rather an apologetic attitude to this treatment in relation to the mother, but this is unnecessary for the following reasons. First and foremost, the extensive use of expectant treatment has produced maternal as well as foetal results as yet unequalled, as recorded by Johnson (1945, 1950), Macafee (1945, 1949, 1950), Mills (1948) and the series now under review. Formerly there was the temptation to examine without delay the patient who had been bleeding, or to operate upon her before she had fully recovered from haemorrhage or shock. Johnson (1950) and others have stressed the danger of performing section on a woman already shocked. With the emphasis now on a more conservative approach, there is usually ample time for the clinical problem to be carefully assessed, not only in respect of the existing emergency, but in relation to the previous health of the patient, and the chance of improving her condition before delivery takes place. For example, a woman with anaemia and a placenta previa is like a man with a depleted bank balance. An unexpected but small demand on already low reserves may bring disaster, as occurred in the case which first aroused our interest in these problems. The mother, as well as the foetus, benefits if delivery is deferred until such time as the chances for both are at their maximum, although it will be appreciated that there are occasions when persisting bleeding necessitates immediate action. An additional important point requires mention. It is not uncommon to find the obstetrical position alter so completely during the weeks of waiting, that whereas cesarean section seemed probable when the patient was admitted, it becomes unnecessary by the thirty-eighth week. The head which was high, or in the iliac fossa at the thirty-second or thirty-fourth week, may well be through the pelvic brim several weeks later, and it may even be safe in selected cases to allow the patient to return home to await spontaneous labour. This is most likely to occur when the placenta is anterior. We do not as yet advocate this procedure in teaching our students, because its safety depends on the careful selection of patients, which is not a task for the inexperienced. We believe it is a safe practice, however, when the head is engaged in the last weeks of pregnancy, the patient is in good health, and she is returning for institutional delivery. It is interesting to note that in the

two series reported by Johnson (1950) the incidence of section was 53 per cent in the first series, with a foetal wastage of 30 per cent, whereas in the later series the section rate was only 42 per cent and the foetal mortality was reduced to 14.7 per cent. The dramatic improvement of already good results was achieved in spite of a reduced use of cesarean section.

Even these facts do not portray the whole picture, because with the old method of immediate interference vaginal examination searching for the placenta was responsible for many premature labours, and a high neonatal death rate, in women whose bleeding was not due to a placenta praevia. These babies are saved by the improved methods of diagnosis and treatment.

The way in which new techniques can assist in the selection of cases for admission to hospital and expectant treatment, has already been discussed in some detail. The patient suspected of having a placenta praevia because of a high presenting part, malpresentation, or haemorrhage, can in most cases have the provisional diagnosis confirmed or disproved radiologically. This can often be accomplished as an outpatient procedure. Furthermore, many of those admitted as emergency cases, without preliminary radiological investigation, can have placenta praevia excluded after admission without a vaginal examination being made. In the last 18 months 25 women admitted to my department because of a suspected placenta praevia were discharged without vaginal examination, and with the pregnancy uninterrupted, after the radiologist had reported a normally situated placenta. In none of these has the subsequent clinical behaviour of the patient challenged the wisdom of this action. It should be noted however, that a point common to all was that the presenting part was engaged, or at least nestling into the brim, before the patient was discharged.

3. Selection of Cases for Treatment

Those in whom the provisional diagnosis of placenta praevia was confirmed by the radiologist were treated expectantly, with the precautions already described, until the thirty-sixth to thirty-eighth week, unless persisting or severe haemorrhage made interference advisable before this. In only 23 cases (13.5 per cent) was this necessary. A practical point which requires emphasis is that during the expectant period the obstetric position may be altered by the presenting part descending into the pelvis. When the maximum diameter is through the brim, if the foetal heart is steady, we consider the immediate danger to the mother and baby is over. If the remainder of the obstetric picture is satisfactory the patient is discharged to await a spontaneous delivery, subject to the conditions previously outlined. Attention to the foetal heart is particularly necessary when the placenta is posterior, because of the danger of a cord of low insertion being compressed as the head enters the brim. When this is suspected by persisting foetal heart irregularity as the head is gently forced into the brim, either by abdominal manipulation or by uterine contractions, oxygen is immediately administered to the mother and section is performed whatever the relation of the placenta to the cervix.

In Macafee's series a low insertion of cord was responsible for 30 in the 47 deaths, and in this series section was performed four times with living infants in the last 100 cases because of this sign of foetal distress. At operation the low attachment of cord was confirmed in each instance, there being direct pressure by the foetal head as it entered the brim. It should be noted that all four cases were considered otherwise suitable for vaginal delivery. In other words this complication can be diagnosed in time to save the foetus and is an indication for cesarean section. A low insertion was confirmed in many other cases at operation for a posterior placenta praevia but when the head could not engage the cord was saved from direct pressure and foetal distress did not result.

If intervention was not made necessary by recurring or severe haemorrhage, and if the presenting part was still not engaged by the thirty-sixth or thirty-eighth week the patient, prepared for section, was examined in the theatre, unless there was thought to be only a mild degree of placenta praevia and the presenting part was becoming progressively more stable at the brim. In such cases interference was not practised unless bleeding occurred, particulary if the placenta was situated anteriorly. The exact stage of gestation from the thirty-sixth to thirty-eighth week at which the examination was made varied according to the size of the foetus, and the degree of placenta praevia as suspected clinically and reported by the radiologist. The findings on abdominal examination were important in making this decision. For example, with a persistent malpresentation, such as a transverse lie or oblique lie, suggesting a total placenta praevia, the tendency was to examine earlier than with a longitudinal lie and a head which felt it might still enter the brim. Fifteen to thirty minutes before the patient was anaesthetised a drip transfusion was commenced into a hand vein. In this way any reaction was not masked by anaesthesia, and when a hand vein was used the arms could be folded across the chest if section was necessary. Except in certain emergency admissions transfusion was not immediately required, but as it increased the margin of safety if severe bleeding occurred during examination or delivery, it was used as a routine when a patient not in labour was examined for placenta praevia.

Vaginal examination was primarily for the purpose of seeing whether the presenting part could be made to enter the brim, and *not to find where the placenta was in relation to the os* (Fig. 14). In fact, it is now our practice to dispense with vaginal examination if the provisional diagnosis has been made by both abdominal palpation and soft tissue radiography, and the presenting part cannot be made to enter the brim by abdominal manipulation. When doubt exists a vaginal examination is made. *We believe that in placenta praevia it is of much greater importance to know where the presenting part is in relation to the brim, than where the placenta is in relation to the os.* It is suggested that this concept of the problem has not been appreciated as widely as it deserves. From this series illustrations have been given in accurate scale

drawings to show how dangerous even a Type 1 or low-lying placenta can be when it is situated posteriorly. A different aspect of the same problem is illustrated by Fig. 15 in which a head of 9 cm. biparietal diameter is shown in relation to three pelves of different sizes, and a placenta of constant thickness. There is major disproportion in pelvis A and ample room in pelvis C.
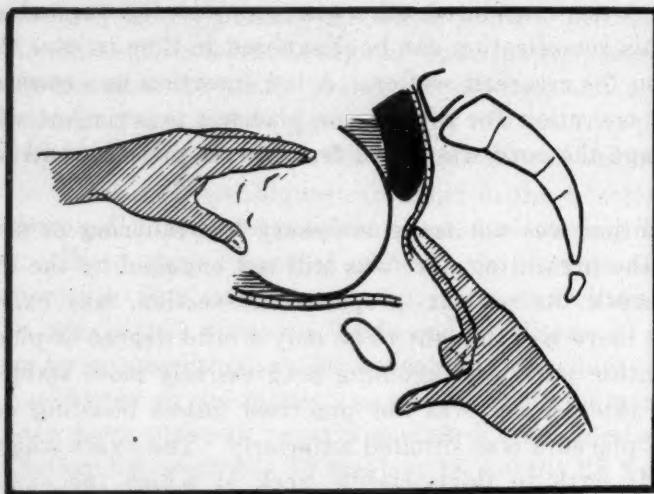
Fig. 14.
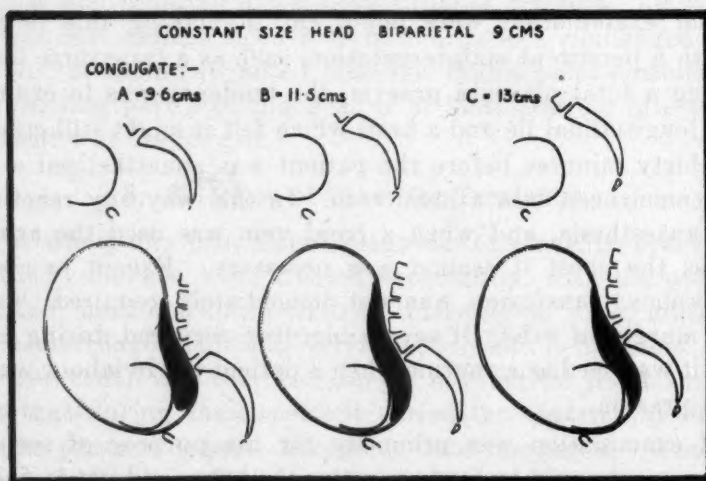
Fig. 15.

The generally accepted teaching that treatment is dictated by the placental position in relation to the os, with its implication of routine vaginal examination, can cause much trouble and many deaths, especially foetal, but sometimes maternal. The more inexperienced the doctor who inserts his finger through the cervix, the more dangerous the practice becomes. Violent haemorrhages can be provoked by one who lacks the skill to save the patient's life. It is our belief that when digital exploration of the lower segment to deter-

mine the placental site is generally abandoned, and with it those classifications of placenta praevia which demand this dangerous practice, there will be a further dramatic fall in maternal deaths from antepartum haemorrhage.

If the head can be made to enter the brim, and feel stable there, the forewaters are ruptured. The foetal heart is closely watched from then until delivery. On several occasions in this series rupture of the membranes was followed later by lower segment section because of either foetal distress, or further bleeding before labour commenced. The fear threshold in respect of lower segment section in infected or potentially infected cases seems to vary on the two sides of the Atlantic. In the last ten years, in the department from which this work is published (which handles a great deal of emergency obstetrics) there have been no deaths from sepsis following section, in spite of the fact that many of the operations were performed on infected or potentially infected women. Marshall (1939) has published a large series with equally gratifying results, and there is widespread confidence in this operation throughout the clinics of the British Isles. For that reason we do not perform the Porro operation, which appears to be more popular in America than in Great Britain.

If the head cannot be made to enter the brim section is at once performed. This was done in 40 per cent of the whole series, but in 51 per cent of the last 100 cases. In 44 of these the operation was performed at once, but in 7 it was performed later because of foetal distress or because rupture of the membranes failed to control the obstetric position. Lower segment section is favoured as the operation of choice, but because we believe it is futile to sacrifice a patient to an ideal, there are occasions when the classical operation with a low vertical incision is performed. This incision is covered with uterovesical peritoneum and bladder at the end of the operation. Eighty-seven per cent of the sections were by the lower segment technique. Only the two methods of treatment, rupture of membranes and caesarean section, have been mentioned because they were the two usually adopted, although on rare occasions a bag or half breech was used when the foetus was already dead.

Results

There was one maternal death. A woman with an advanced lymphoepithelioma of the pharynx invading the base of the skull and sella turcica, was admitted with a central placenta praevia giving rise to severe haemorrhage at the thirty-fourth week. A lower segment section was performed and recovery was surprisingly uneventful. A week after operation she was transferred to the Ear, Nose, and Throat Department for treatment of the pharyngeal cancer, but she died suddenly of respiratory obstruction several days later. Autopsy cleared the obstetric condition of responsibility for the death but as it occurred in the puerperium it is included here.

In the whole series of 245 the uncorrected foetal wastage was 18 per cent (Table II) while in the group of 170 it was 20 per cent. In the last 100 consecutive cases (Table III) it was 13.7 per cent in 102 deliveries and so far this year there has been one macerated stillborn twin in 22 deliveries.

TABLE II. MODERN RESULTS IN FOETAL SALVAGE

CENTRE	NUMBER	DEATHS UNCORRECTED	FOETAL WASTAGE	CAESARIAN INCIDENCE
Houston (Johnson)	201	43	21%	46%
Belfast (Macafee)	275	56	20%	46%
Oxford (Stallworthy)	245	44	18%	40%

TABLE III. FOETAL SALVAGE IN THE LAST HUNDRED

| CENTRE | NUMBER | | DEATHS | FOETAL WASTAGE | CAESARIAN INCIDENCE |
	CASES	FOETUSES			
Houston (Johnson)	122	122	18	14.7%	42%
Birmingham (Mills)	100	103	17	16.5%	47%
Oxford (Stallworthy)	100	102	14	13.7%	51%

Summary

The ideal for which we strive is no maternal deaths, and a foetal wastage of less than 10 per cent.

1. We believe this can be obtained by teamwork starting in the antenatal clinics and involving the obstetricians, the radiologists, the paediatricians, and last, but not least, the nursing staff.

2. The radiologist is of particular value in helping to select those patients suitable for expectant treatment, and in avoiding the unnecessary hospitalisation of those without a placenta praevia. When skilled staff is not available for soft tissue placentography, a simple lateral film of the pelvis can be of use.

3. Anaemia must be detected early and adequately treated, and from then on the watchword is, "Avoid haemorrhage."

4. Expectant treatment is possible in over 80 per cent and should reduce the foetal mortality to the level of 10 per cent or less.

5. It is claimed that this treatment when carefully supervised also improves the maternal prognosis.

6. The more cases of placenta praevia detected in the antenatal clinic before haemorrhage occurs, the better will be the results for mother and babe.

7. In any large series it should be possible to admit to hospital at least 20 per cent of women with placenta praevia before there is any haemorrhage.

8. Caesarean section has an important place in the modern treatment of the condition, but only a place. It is the method of choice in approximately 50 per cent of cases.

9. The selection of these depends on the relation of the presenting part to the brim of the pelvis, more than on the position of the placenta in relation to the cervix. When the presenting part will not engage rupture of the membranes may lead to disaster for both mother and babe.

10. The posterior placenta was the most common one in this series.

11. It is claimed that the dangerous placenta is not the total one or Type 4 as is commonly taught, for concerning the treatment of this there is little dispute. Greater danger lurks in the low-lying Type 1 or 2 placenta when it it posteriorly situated. Although so little praevia as to be out of reach of all but the most experienced fingers, it may prevent engagement of the presenting part and by so doing render difficult or impossible the adequate control of bleeding by the vaginal route.

12. With this type of placenta there is an increased hazard of cord compression. It can be diagnosed in time to save the foetus and is an indication for caesarean section.

In conclusion it can be said with truth that this Oration has provided fresh confirmation of the old adage, "There is nothing new under the sun." It has, however, sought to give emphasis to certain practical concepts of an important clinical condition. Where it has challenged current teachings and practices, it has done so only after much thought and considerable research, but time alone will tell whether the challenge will be supported by the accumulated experience of other clinicians.

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RESECTION OF THE SUPERIOR HYPOGASTRIC PLEXUS*

Modification of the Technique to Prevent Regeneration

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SINCE the publication of my first paper[1] (read before the A.M.A., Section on Obstetrics, Gynecology and Abdominal Surgery) on relief of pelvic pain by sympathetic neurectomy in 1933, and my second communication,[2] read before this Association at its annual meeting in 1934, I have closely followed the reports of other authors.

Also, I have observed several operators doing resections of the superior hypogastric plexus. I have noted, in the literature, that incomplete resection is repeatedly blamed for recurrence or persistence of dysmenorrhea. In some instances, regeneration of the plexus is suggested as the cause of reappearance of symptoms months after operation. These observations have prompted me to bring to your attention a modification of the technique which should prevent regeneration between the cut ends of the plexus. The modification was first utilized in 1941. With complete resection and use of the suggested modification, in properly selected cases, the good end-result percentages should be higher.

In the excellent "Oration"[3] given before this body in 1948, O'Donel Browne, Master, The Rotunda Hospital in Dublin, has given us criteria for the proper selection of cases and, for ovarian dysmenorrhea, advocates section of the ovarian plexus in the infundibulopelvic ligament. His method of case selection, with section of the ovarian sympathetic nerve supply when indicated, plus proper resection of the superior hypogastric plexus, with the added modification, seems at this time to be close to the attainment of perfection.

But such attainment will be dependent upon individual abilities. Errors in technique easily pass through generations of surgeons. With this in mind, I here present, in detail, what I believe to be important steps in the total ablation of the superior hypogastric plexus.

Details of Steps of Operation With a Modification

1. The patient should be in extreme Trendelenburg position.
2. Spinal anesthesia is best in that it decreases the bulk of the intestinal tract. This often allows the operation to proceed without the need of packing away the ileum and colon. If packing is necessary, a piece of rubber dam is placed over the gut *before* gauze packing is used. This is to prevent the possibility of adhesive-band obstruction due to injury of delicate endothelial surfaces. This simple preventive was advocated many years ago by Dr. John

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Keefe of this Association. (His admonition is apparently followed only by those who have had to return a patient to the hospital for relief of obstruction a few months after a pelvic operation.)

3. The umbilicus lies in front of the fourth lumbar vertebra. There the aorta divides. An incision which extends upward to a point approximately 5 cm. above and to the left of the umbilicus eliminates forceful upward pulling and hauling on retractors during the topmost portion of the resection.

4. After the operative field is exposed, the point of bifurcation of the aorta is determined by sense of touch. Then, halfway between the promontory of the sacrum and the bifurcation, the posterior parietal peritoneum is picked up between two toothed thumb forceps and a small vertical incision made into it with a knife. Now, keep in mind the fact that many fibers of the plexus hug the posterior surface of the peritoneum. A gently curving pair of slender scissors is inserted into the incision, curve pointing anteriorly, and the blunt point of the scissors carried upward while pressing firmly against the peritoneum. The scissors are opened a bit during each forward thrust. This maneuver is then repeated in a downward direction. Thus a path about 1 cm. wide is made, upward to a point approximately 5 cm. above the bifurcation and downward to the level of the sacral promontory or just below it. (It is at this lower level that the superior plexus divides into the two inferior groups, which are to be avoided.) The peritoneum is then incised with straight scissors along the center of the prepared path.

5. The operator is now enabled to grasp the edges of the incised peritoneum with hemostats and begin his dissection by freeing the tissues adherent to the posterior surface of the peritoneum by blunt dissection with pledgets of gauze held in an instrument. This cleaning is carried laterally to the lateral margins of the common iliac arteries and upward and downward to the points previously indicated. Lack of meticulous dissection at this stage of the operation may be the reason for some of the failures which are reported.

6. With the peritoneum clean, the tissues containing fine nerve fibrils, now mobilized, are picked up with a hook and the common iliac arteries and left common iliac vein are cleaned with cotton or gauze pledgets in a holder. As these nerve-containing tissues are freed they are repeatedly picked up with blunt hooks and placed in the larger main bundle which is accumulating and which may well be held in the grasp of one or two Allis clamps. (This is one of the few purposes for which I have found this clamp useful.) During the lateral portion of the dissection, the surgeon must be alert in recognition of fine nerve fibrils coursing into the area from right and left, both over and under the vessels. These fibrils, sometimes as small as the finest strand of a spider's web, and coming from the fourth, and sometimes higher lumbar ganglia, if missed, add another cause for failure. As I have pointed out before, a dry field is of great importance. The small fibrils suddenly become visible after heavy pressure with a gauze sponge on a holder. Repeated drying is an essential to meticulous dissection. The main bundle of the plexus is cleaned away from the vertebrae and lifted forward. The entire group of fibers now may be held as suggested, and moved from one side of the field to the other, while further search is made for missed fibrils.

7. In the area above the aortic bifurcation, the left intermesenteric nerve sends fibers to the left along the inferior mesenteric artery. They should be included in the dissection because they may branch and find their way into the plexus at a lower level.

8. When the operator is satisfied that his dissection is complete, the bundle is grasped with a heavy hemostat, above, at a point approximately 3

cm. superior to the aortic bifurcation, below, at the point where it spreads out into its "bifurcation" to form the inferior hypogastric plexus, and the dissected portion removed. The crushed ends are transfixed and tied.

Modification

9. At this stage I have modified the usual technique which closes the peritoneum after cutting away the dissected portion of sympathetic nerve fibers and leaves both ends behind the peritoneum. (The actual fact of regeneration of the superior hypogastric plexus following its resection has not, to my knowledge, been reported in the literature, but regeneration of resected sympathetic nerve fibers elsewhere in the body has been frequently noted.)

With the proximal stump held forward by a hemostat, or, if desired, by the ends of the transfixion suture which has been left long, closure of the peritoneum is begun at the upper end. I use a No. 00 plain catgut suture, doubled, for this purpose. This suture firmly closes the peritoneum around the upper stump. A transfixion stitch is now passed through the peritoneum and stump, at the point of emergence, and the peritoneal closure continued with a running stitch. The ends of the nerve fibers of the proximal stump now lie in the abdominal cavity; the lower stump is buried behind the peritoneum.

Summary

A modification of the usual technique of resection of the superior hypogastric plexus is presented. Its purpose is to prevent regeneration of the plexus between the cut ends.

Details of the entire technique which have aided the author in obtaining complete ablation of the plexus are described.

References

1. Wetherell, F. S.: J. A. M. A. 101: 1295, 1933.
2. Wetherell, F. S.: AM. J. OBST. & GYNEC. 29: 334, 1935.
3. Browne, O'Donel: AM. J. OBST. & GYNEC. 57: 1053, 1949.

Discussion

DR. LOUIS E. PHANEUF, Boston, Mass.—In the management of severe or intractable dysmenorrhea, when the conservative methods have failed, operations on the sympathetic nervous system usually give satisfactory results in controlling the crippling pain that accompanies menstruation. Leriche of Strasbourg practiced periarterial sympathectomy, this intervention consisting of the resection of the adventitia of the hypogastric and ovarian arteries on each side, and obtained good results, especially in ovarian dysmenorrhea. He published his results in the *Presse Médicale*, Paris, April 11, 1925. Since 1924, G. Cotte, of Lyon, France, has practiced exclusively the resection of the superior hypogastric plexus of Hovelacque for the severe forms of dysmenorrhea. His technique is described in his book: *"Troubles fonctionels de l'appareil génital de la femme,"* third edition, Paris, 1949, Masson & Cie, and alo in the *American Journal of Surgery*, Vol. 78, No. 1, July, 1949.

The operation of presacral neurectomy is intended for primary or essential dysmenorrhea and not for ovarian dysmenorrhea. The best results are therefore obtained by the careful selection of the patients. In the presence of ovarian dysmenorrhea, O'Donel Brown of Dublin and the essayist advocate the resection of the ovarian plexus in the infundibulopelvic ligament, in addition to the resection of the superior hypogastric plexus.

Dr. Wetherell describes his technique in detail, and proposes extending the abdominal incision upward, 5 cm. to the left of the umbilicus. There is no question but that this generous incision facilitates the dissection and prevents trauma to the abdominal wall. His careful dissection, and his recognition and resection of all small fibrils, which are frequently overlooked, doubtless add to his good results. His modification of the operation, whereby he leaves the superior end of the resected presacral membrane outside of the peritoneum, and buries the inferior end, should, and does, prevent the regeneration of the nerve elements, an admitted source of recurring pain.

From Dec. 4, 1933, to March 4, 1950, I have done 134 presacral neurectomies. Follow-up results were not obtained in 11 cases, leaving 123 cases for study.

The results were as follows:

Total number of satisfactory cases, (pain completely relieved)	80, or 65 per cent
Total number of improved cases, (very slight pain)	28, or 22.7 per cent
Total number of unimproved cases,	14, or 11.3 per cent
Death,	1, or 0.8 per cent

After necropsy, the death was ascribed to anesthesia. A total of 108 patients, 87.7 per cent, were entirely relieved or had very slight pain following operation.

In all of these cases the presacral membrane was examined histologically and myelinated and nonmyelinated nerve fibers and nests of sympathetic ganglion cells were reported.

In Gaston Cotte's paper, published in the *American Journal of Surgery*, July, 1949, he reported over 1,500 operations with recurrence of symptoms in 2 per cent of his patients.

Dr. Wetherell's modification in the technique of operation appears to me to be an important one, and one that should improve our results in the performance of this intervention.

DR. J. P. GREENHILL, Chicago, Ill.—As is well known, Dr. Wetherell was one of the pioneers in the use of resection of the superior hypogastric plexus for the relief of dysmenorrhea. I began performing resection of the superior hypogastric plexus in 1931, and since then I have done many of these operations for the following four indications.

1. Primary dysmenorrhea, but only in patients in whom all the customary treatment, including analgesics, exercise, estrogens, and minor surgical procedures, have failed. The results in these cases have been excellent.

In 1924, Cotte showed that pain arising in the midpelvic organs could be relieved by resecting the superior hypogastric plexus. In 1929, L'Hermitte and Dupont and independently Leriche suggested that a painful ovary could also be rendered insensitive by denervation. These authors soon realized that, owing to the cross link in the nerves between the ovaries, bilateral denervation was necessary for success. Their most recent technique is division of the two or three main ovarian nerve bundles in the mesovarium without interfering with the ovarian blood vessels. O'Donel Browne also advocates ovarian sympathectomy in cases where the menstrual pain is of ovarian origin. He determines this by firm bimanual compression of the ovary while asking if the pain or discomfort thus produced is similar to that experienced at the menses. Browne's technique for ovarian denervation consists of simple division of both infundibulopelvic ligaments, their nerves, and blood vessels, and simple ligature of the stumps with catgut.

In 1939, Cooke operated on women under local infiltration anesthesia to determine the routes of pain conduction. From the standpoint of the relief of dysmenorrhea, he drew the following conclusions in regard to the various types. In the cramping (uterine) type, presacral sympathectomy is wholly adequate; in the congestive (vascular) type, no effective nerve section has yet been devised; in the ovarian type, ovarian sympathectomy should be done, and in the peritoneal type, no operation is available for the areas outside the distribution of the presacral and ovarian plexuses.

2. Endometriosis in young women at the time of a conservative operation is a second indication for pelvic sympathectomy. Whether the sympathectomy has any beneficial effect on the endometriosis is questionable, but it does reduce pain in the cul-de-sac, utero-sacral ligaments, and bladder following the operation. Also, it will prevent a good deal of pain if there is a recurrence of endometriosis and it will diminish pain during labor. This operation will not eliminate pain in the ovaries due to endometriosis unless the ovarian vessels are ligated and cut.

3. Pain due to carcinoma is a third indication. Pelvic sympathectomy will almost completely relieve the intractable pain in about half the women who have advanced carcinoma of the cervix. However, intraspinal injection of alcohol is simpler and effective in more cases. Nevertheless, at the time of laparotomy for carcinoma of the cervix or the corpus, it is advisable to perform resection of the superior hypogastric plexus because should there be a recurrence of the carcinoma, the pain will be less intense than if the sympathectomy had not been done.

4. Sympathectomy may also help in rare cases of severe persistent pain in the lower abdomen not relieved by so-called exploratory operations which failed to reveal a cause for the pain. In these cases, pelvic sympathectomy may bring dramatic relief from the pain, provided the patient has not developed a psychosis about the pain.

The technique which most of us use is that described by Cotte, and we try to remove every single nerve fiber connected laterally with the superior hypogastric plexus. I remove the two hypogastric nerves which rest on the sacrum, as well as the superior hypogastric plexus which lies on the lower lumbar vertebrae, and I do not tie the ends of the nerve tissue which is left behind. The piece of nerve tissue which I remove is at least 6 cm. long, and even though it is hard to believe that regeneration of the nerve tissue can take place across such a distance, such a possibility nevertheless exists. Therefore, Wetherell's modification is a distinct improvement in the operation.

Every piece of tissue which is removed during a pelvic sympathectomy should be examined microscopically to be certain that nerve tissue and ganglia are present. Not infrequently an inexperienced surgeon will have a failure due to the fact that no nerve tissue was removed, only fat and connective tissue. Of course, such a failure cannot be charged to the operation.

Pelvic sympathectomy is generally a fairly simple operation, but there are some dangers, particularly to the ureters and to the large blood vessels. Because the operation is usually easy and the results are excellent, it is being used too often for cases of dysmenorrhea which do not require a laparotomy. However, when the abdomen is opened for any reason in women who have severe dysmenorrhea, the superior hypogastric plexus should be removed as an accessory operation.

DR. WETHERELL (Closing).—The reason I mentioned the length of the incision is because in my own experience I often had to have a great deal of retraction trying to get the upper end of the plexus. Dr. Charles Mayo said, years ago, that an incision heals from side to side and not from end to end, so why not give ourselves room. I still do not like the term ''presacral.'' This plexus lies on the lower lumbar vertebrae, not in front of the sacrum. I was glad to hear Dr. Greenhill say that he and his group obtained relief of pain in 50 per cent of their cases of carcinoma. My first paper included reports of cases in which I had done the resection for relief of pain in carcinoma. That report was given adverse comment in the volume on the sympathetic nervous system by White and Smithwick. The remark is made that Adson, Wetherell, and others have advocated superior hypogastric plexus resection for the relief of pain in pelvic carcinoma but it is of no value. I asked Smithwick to delete those words from his next book because I myself had obtained no relief in several successive cases following my report. Perhaps in those early days the operation was not as complete as it is now. We may have to alter our views.

SARCOMA OF THE ENDOMETRIUM*

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THE purpose of this communication is to report three new cases of an invasive growth arising in endometrial stroma, to give a follow-up report on a case reported in 1942 by Chester Brown, to draw attention to the apparent sensitiveness of this condition to radiation, and to discuss the implications presented by these cases and two others of a different type in reference to the terminology of this condition.

CASE 1.—The patient was an unmarried woman of 32 years whose previous history was uneventful. Her periods began at the age of 14 years and were regular in frequency, duration, amount, and character until November, 1930, when there was an abrupt increase in the duration from five days to sixteen days. Menorrhagia continued to May, 1931, at which time the uterus was found to be symmetrically enlarged to the size of a ten weeks pregnant uterus. At curettage an irregularity in the fundus was felt. The diagnosis of submucous fibromyoma was made. The uterus was irregularly nodular and was removed supravaginally. The cut surface showed two typical sharply demarcted myomas. The principal enlargement of the uterus was due to a mass of tissue which on the endometrial surface was irregularly nodular and spread from there toward the surface of the uterus as a fan-shaped area without clear demarcation, roughly 5 cm. in diameter. The surface was finely granular, almost smooth, of a homogeneous gray color crossed by hemorrhagic steaks which radiated more or less from the endometrium outward. The consistence was softer than that of the surrounding uterus but not very friable.

Histologic Examination (Fig. 1).—The endometrium consisted of a single layer of columnar cells beneath which the glands appeared normal in size, shape, and distribution. The stroma appeared normal. The uterine wall was composed of interlacing strands and bands of smooth muscle and connective tissue fiber. Scattered in the uterine muscle were small infiltrating islands of tissue, similar to endometrial stroma, but whose cells varied in size and shape although remaining typically spindle shaped. The nuclei stained more deeply than the normal endometrial stroma. No glands were seen. Some clumps of cells occupied the lumen of lymph vessels and blood vessel wall. A number of mitotic figures were seen in some places; in others none. Sections through the nodular projection into the uterine cavity showed at one point a small area covered by a single layer of columnar cells. Most of the projections were undifferentiated and composed of young stroma cells seen between the muscle bundle of the myometrium.

Diagnosis.—Spindle-cell sarcoma of the uterus (endometrium). This diagnosis was confirmed by Dr. Robert Meyer.

The patient was symptomless and had no follow-up examination until May, 1934, when a mass about 1 cm. in diameter was noticed in the lower angle of the abdominal wound. This was firm, fixed, and bluish in color. It was excised and proved to be of the same nature as the original uterine mass (Fig. 2). At this time the pelvis was clear.

In the summer of 1935 she began to have vague abdominal discomfort and incomplete bowel evacuation. In October signs of partial intestinal obstruction appeared, abdominal

cramps, nausea and vomiting, and absence of stools. On examination there was found a mass fastened to the left wall of the pelvis, extending well beyond the midline and up beyond the pelvic brim into the abdomen, roughly 10 or 12 cm. in diameter, irregular in shape, nodular, hard, and absolutely fixed. Three-positional x-rays showed only the widely distended descending colon which was not considered characteristic of intestinal obstruction.

Intravenous pyelograms showed absence of activity of the left kidney. Diagnosis of obstruction of the sigmoid and left ureter was made. Oct. 14, 1935, a sigmoidostomy was performed above the point of obstruction which was caused by a constriction of the pelvic colon by the mass which also extended up retroperitoneally in the left posterior abdomen. She was given x-ray therapy from Nov. 1, 1935, to Jan. 22, 1936, to five ports, two anterior, two posterior abdominal and one lateral field, a total of 10,054 r to the skin measured in air. Factors were 200 kv., 80 and 50 cm. anode skin distance; filter 2 mm. Cu., 1.0 mm. Al.

There was a rapid diminution of the mass. The spur of the colostomy retracted. Normal bowel movements ensued. On March 5, 1936, the colostomy was closed. At this time there was very little of the pelvic mass remaining but there persisted up into the kidney region induration of a less amount than originally felt but still definite. She was given additional x-ray of 1,400 r to one anterior and one posterior field.

She was followed regularly, had several admissions to the hospital for colds, chronic cystic mastitis, and local infections. In 1946 intravenous pyelograms showed that the lumen of the left ureter had been restored. Barium enema showed complete restoration of the lumen of the bowel with a slight irregularity at the site of the colostomy. There was no pelvic or abdominal mass or induration.

April 7, 1947, she was admitted with a diagnosis of grippe. Local signs were negative except that the breasts began to swell. Biopsy of the breasts revealed myelogenous leucemia which led to her death, July 29, 1947.

This is a case of a growth in the endometrium which metastasized to the abdominal wound, recurred in the pelvis, extended retroperitoneally along the posterior abdominal wall as far as the left kidney and caused obstruction to the rectosigmoid and the left ureter. Under x-ray therapy the mass disappeared, the lumen of the bowel was restored, and function of the left kidney resumed. There was no further evidence of disease for eleven years when she died of another disease.

CASE 2.—This is the case reported by Dr. Chester Brown[1] of a woman, aged 46 years, who, in August, 1938, was admitted to the Lincoln Hospital with a history of six months' metrorrhagia and a uterus the size of a three months' pregnancy. A diagnosis of fibromyoma was made and a complete hysterectomy and left salpingo-oophorectomy were performed. The uterus was diffusely enlarged by a yellowish mass of tissue. The endometrial cavity contained many small polyps.

Histologic examination was essentially the same as that in the previous case.

We wish to report her subsequent history which revealed that in 1939 she was operated upon for intestinal obstruction. She came to us July 20, 1940, with pain in the lower abdomen, loss of flesh and strength, and constipation. On examination, the pelvis was filled by a mass extending from wall to wall, fixed, nodular, hard, and slightly tender. There was a slight leucocytosis. The patient appeared moderately cachectic. Because of the apparent hopelessnes of the situation, she was about to be referred out for terminal care when the experience of the case reported above was cited. For this reason she was given a course of intensive x-ray therapy to the pelvis from Feb. 7 to June 28, 1941. Despite the discomforts of the x-ray therapy her strength gradually returned so that she was able to go about freely after about three months. There was a progressive shrinkage of the mass which, however, did not disappear completely until June, 1947. She was last examined Oct. 20, 1949, at which time the pelvis and abdomen were free of masses or induration. Her general condition was excellent.

CASE 3.—One other case is reported for the record. A 43-year-old woman suffered for 5 months from excessive menstruation. A dilatation and curettage were performed and the

Fig. 1.
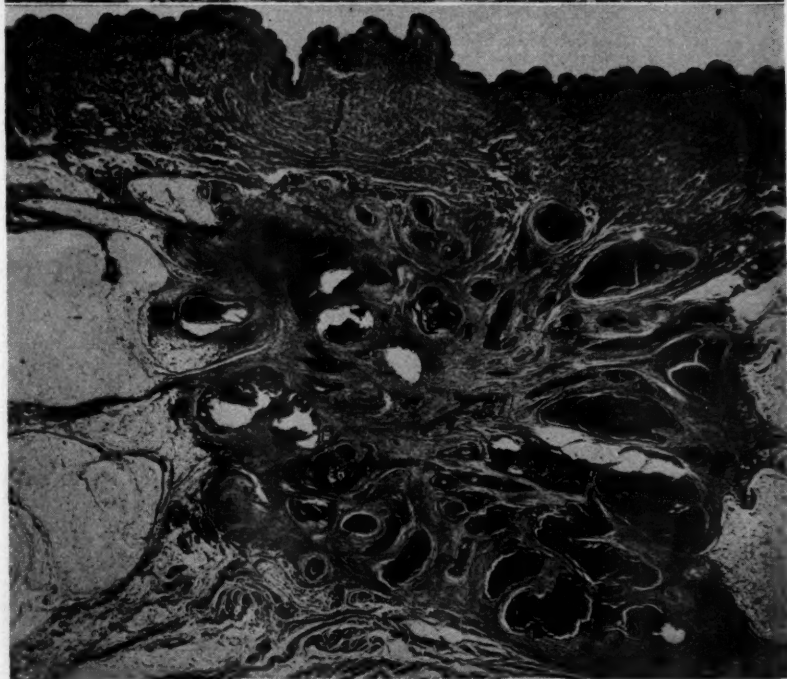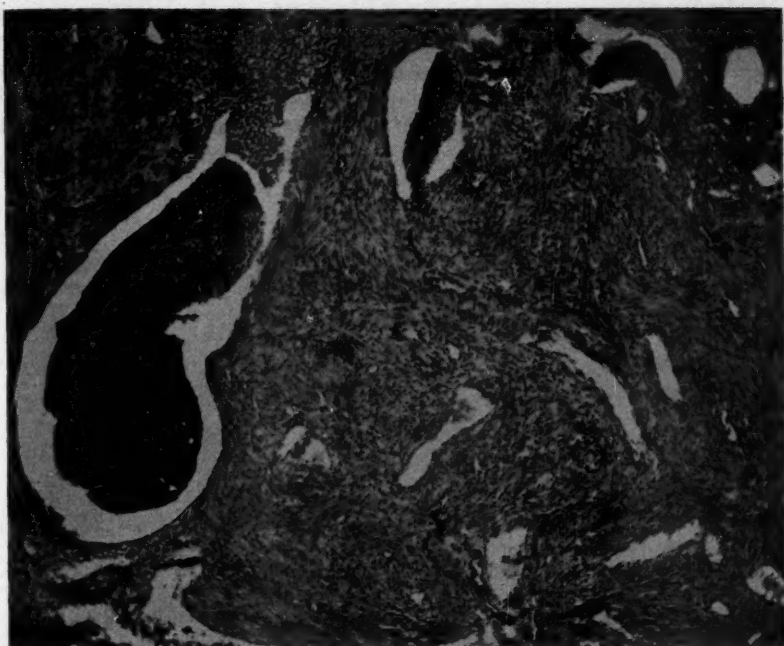
Fig. 2.

Fig. 1.—Photomicrograph of uterine wall in Case 1 showing the endometrial stromalike tissue. There are spindle cells which vary in size and shape. The nuclei are large in proportion to the cytoplasm, hyperchromatic, and contain a few mitoses. Clumps of cells fill vascular spaces and in spots seem to spring from the vessel wall.

Fig. 2.—Photomicrograph of metastatic tumor removed from the abdominal scar three years after hysterectomy in Case 1. The histologic characteristics are similar to those of the original lesion.

patient told she had a submucous myoma. At our examination the uterus was symmetrically enlarged to the size of a three months' pregnancy. The uterine cavity was smooth. The enlargement of the uterus was caused by a typical intramural myoma which distorted the uterine cavity only slightly. There was no gross manifestation suggesting the presence of the endometrial lesion which was discovered in the microscopic examination and was about 1 cm. in diameter and histologically was identical with those lesions just described. The patient had a complete abdominal hysterectomy and bilateral salpingo-oophorectomy. No postoperative x-ray therapy was given.

Fig. 3.
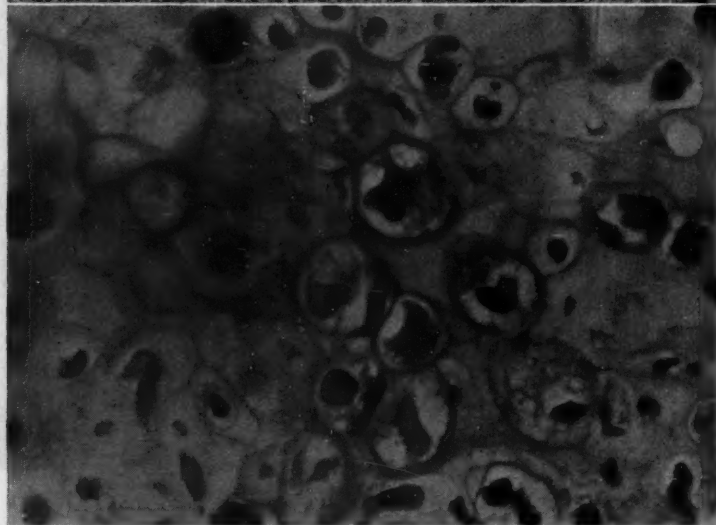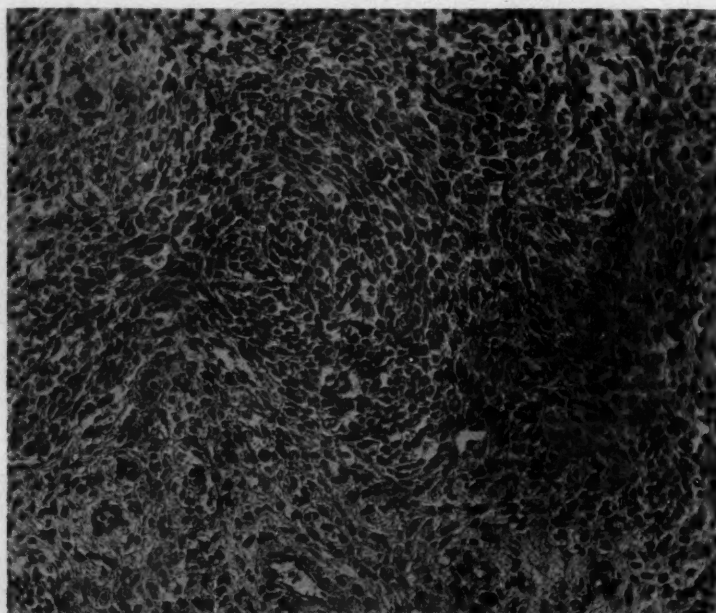
Fig. 4.

Fig. 3.—Photomicrograph of a polypoid endometrial tumor, Case 4. The cellular arrangement is much more irregular than in the previous case. There is greater variation in size and shape of the cells and of their nuclei. The tumor tissue is sharply demarcated from the myometrium.

Fig. 4.—Photomicrograph of a piece of cartilage in the neoplastic tissue of Case 4.

CASE 4.—Another case of a tumor arising in the endometrium is reported because the growth was endometrial but with characteristics different from those in the cases previously cited. A woman, aged 58 years, gravida vi, para iii, ceased menstruating in 1940. In March, 1948, she began to have irregular vaginal bleeding, increasing in amount. At operation on June 19, 1948, a bilateral salpingo-oophorectomy and complete abdominal hysterectomy were performed for a right tuboovarian abscess 10 cm. in diameter and a uterus enlarged to the size of a ten weeks' pregnancy. The tuboovarian mass was inflammatory. The uterine en-

Fig. 5.
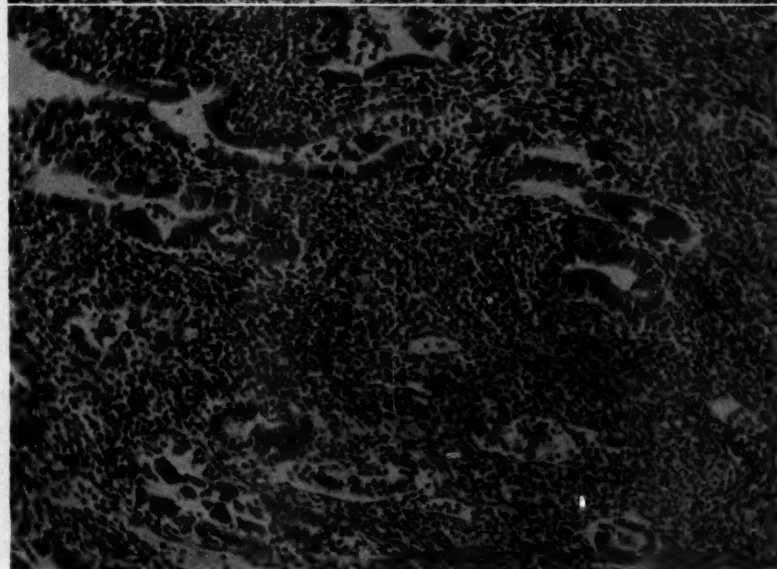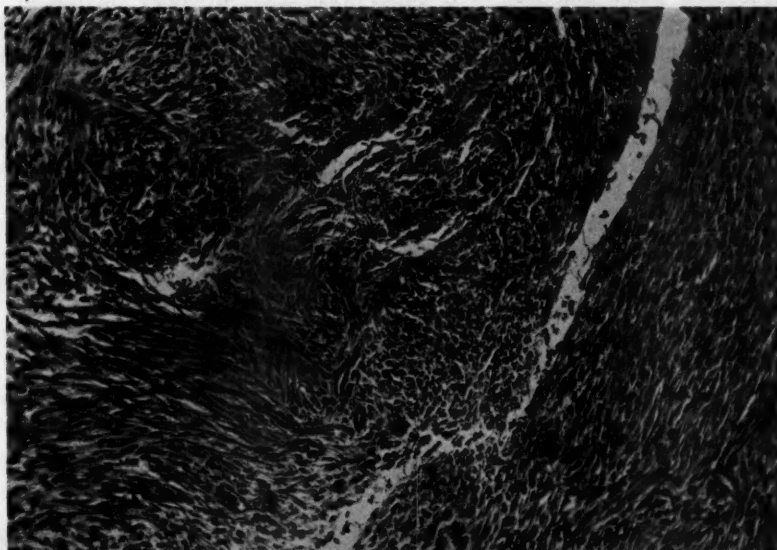
Fig. 6.

Fig. 5.—Photomicrograph of polypoid mass in Case 5. This shows a greater pleomorphism than is seen in the first case. A blood vessel is filled with neoplastic cells.

Fig. 6.—Photomicrograph of a portion of the uterine wall at the base of the polypoid mass in Case 5, showing stromal tissue similar to that seen in the polypoid mass intermingled with adenocarcinoma.

largement was caused by a polypoid mass 11 by 3½ by 2 cm. attached to an area 4 by 3 cm. near the top of the uterine cavity. On cut section it was soft, smooth, of a pink or mottled yellowish gray color with dark red necrotic spots. The mass was sharply limited to the endometrium and sharply demarcated from the myometrium.

Histologic Examination.—The uterine cavity was lined by a thin zone of endometrium, with surface epithelium of columnar cells. Glands and tubules were widely scattered, slit-like and oval, and lined by columnar cells with basal oval nuclei. Stroma consisted of naked-nucleus type cells; showed more than average infiltration with lymphocytes and plasma cells. Sections of the neoplastic polypoid growth, described grossly, showed wild overgrowth of connective tissue cells which had long oval nuclei with finely granular chromatin. The cytoplasm was reticular, faintly eosinophilic and scant, and cell outlines could not be seen. Few mitotic figures, dumbbell shape, and large multilobulated nuclear forms were seen. There were many phagocytes laden with tiny refractile droplets. There were interstitial edema, hemorrhage and necosis in places. Few widely scattered glands were lined by columnar and cuboidal cells with uniform round nuclei and deeply eosinophilic cytoplasm. Some of these glands were cystic. There were two islands of cartilage and adjacent stromal cells showed hyalinization of cytoplasm. Myometrium consisted of bundles of fibromuscular cells haphazardly arranged. It was shaply delineated from adjacent sarcoma except for one short papillary projection which invaded the myometrium.

Diagnosis.—Endometrial sarcoma with cartilaginous metaplasia; chronic endometritis; normal myometrium; chronic cervicitis (Figs. 3 and 4).

She was given routine x-ray for cancer of the pelvis. There has been no recurrence during two years.

The appearance of this tumor is quite different from that of those just described. There was much greater variation in shape and size of the cells, a more disorderly arrangement. The cells did not stain the characteristic deep blue with hematoxylin. The presence of cartilaginous pieces suggests that it should be classed as a teratoma.
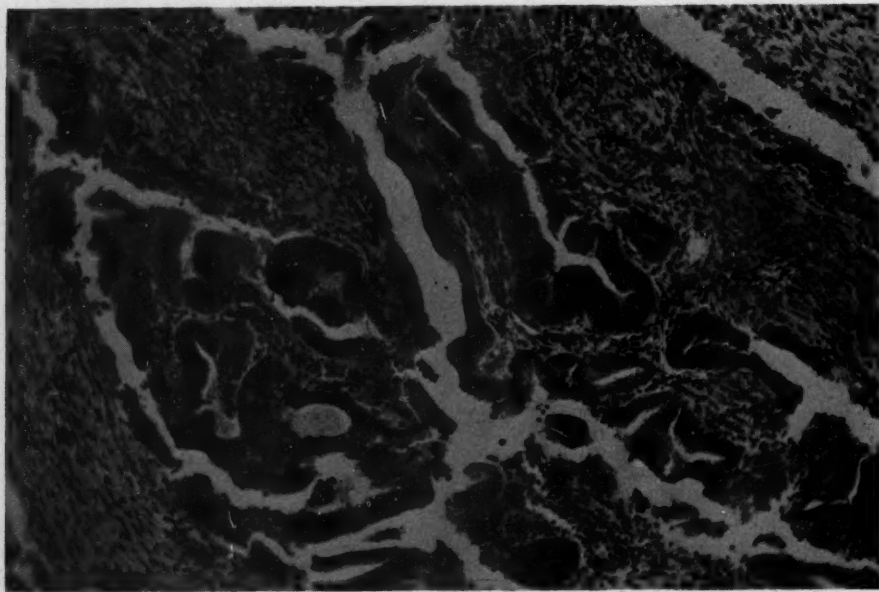
Fig. 7.—Photomicrograph of vaginal metastasis in Case 5. The specimen shows no abnormality of the stroma. The tumor is made up entirely of adenocarcinomatous tissue.

CASE 5.—The following case is reported to stress the point that the sarcoma-like stroma of a carcinomatous growth, although histologically very similar to that of the invasive growths of Cases 1, 2, and 3, lacked the power to invade and in the metastases disappeared entirely,

leaving a pure adenocarcinoma. A patient, aged 55 years, para ii, gravida ii, whose menopause occurred in 1925, had a history of vaginal staining beginning in 1927 and continuing for three years with hemorrhages in early 1929. On March 12, 1929, a mass 6 by 10 cm. was found protruding from the cervix. It was dark red, firm, and in spots necrotic. The mass was excised from within the uterus which was then found to be of average dimensions. The fornices were clear. The histologic examination of the removed mass showed sarcomatous tissue similar to the endometrial sarcoma (Fig. 5) and a diagnosis of sarcoma of the endometrium was made. On March 20, 1929, the uterus, tubes, and ovaries were removed. The uterus was slightly enlarged. There were several small myomas. The base of the polypoid mass, about 3 cm. in diameter, was located in the uterine fundus. Histologically the tumor tissue at the base of the polypoid mass showed the presence of the sarcoma-like stroma intermingled with typical adenocarcinoma (Fig. 6).

This was an adenocarcinoma of the corpus lying at the base of a large polypoid mass consisting entirely of apparently malignant connective tissue cells which were intermingled with the alveoli of the carcinoma. On March 8, 1930, one year after hysterectomy, a mass 3 cm. in diameter was felt to the left of the urinary meatus. On the summit of the mass was an ulcer 1 cm. in diameter. Biopsy showed pure adenocarcinoma (Fig. 7). She was given on March 9, 1930, May 13, 1930, Sept. 29, 1930, and March 4, 1931, a total of 2,300 mg. hr. of radium in a plaque 2.5 cm. by 1.0 cm., 0.5 cm. distance between radium and skin, 1.0 mm. platinum filter. She had no symptoms or physical signs in the pelvis thereafter. In May, 1935, the vagina was clear. A mass 2 cm. in diameter was felt in the left breast. This was a separate carcinoma of the breast from which she died in 1937, at which time there was no evidence of recurrence of the carcinoma of the corpus.

Discussion

Three types of tumor of the endometrium are presented: a growth which resembles the stroma of the endometrium, one which is more cellular and contains cartilage, and a third which is composed of both adenocarcinomatous and sarcomatous elements but which metastasized as a pure adenocarcinoma.

The first type of tumor has been given many names: sarcoma,[2, 3] fibromyosis endolymphatica,[4] stromatous endometriosis,[5] endometriosis interstitialè,[6, 7] etc., all of which imply that there is no neoplasm but simply an infiltration of the surrounding tissue by endometrial stroma minus its glands. The cells resemble those of the endometrial stroma except that they exhibit the usual but mild characteristics of malignancy.

The word-ending "osis" signifies an infiltration by a tissue into the surrounding structures but in a manner which is self-limited. The process stops at a certain point although metastases in regional lymph nodes have been observed.[8] It is, however, benign and may be treated conservatively. Excision is performed for symptoms and is rarely complete. A residue of the disease does the patient no particular harm.

The ending "oma" signifies a true neoplasm which, if it is malignant, is characterized by a profuse lawless growth of cells, invasion, and metastasis, and ultimately destroys the patient.

The term to be used to designate any particular disease depends upon the actual behavior of the growth process. There are many examples in which there is indefinable gradation in the histologic picture from that which is normal to that which is malignant.[9]

Normal pregnancy is composed of undifferentiated tissue which invades the muscularis of the uterus and metastasizes to the lungs. Hydatidiform mole merges indefinably into chorioadenoma destruens which, in a small number of cases, metastasizes.

In carcinoma of the cervix there is no clear-cut border line between normal squamous epithelium, metaplasia, basal-cell hyperplasia, carcinoma in

situ, early invasive carcinoma, and, finally, frankly clinical cancer of the
cervix. Carcinoma of the endometrium can with difficulty be distinguished
from adenomatous hyperplasia (carcinoma in situ, Hertig[10]) and this again
from simple endometrial hyperplasia, there being no clear-cut border line
between the different stages of abnormal cell activity.

In all of these conditions the process is up to a certain point reversible,
that is, the variation from the normal ceases and eventually may disappear.
When the process becomes irreversible, it progresses into true cancer which
has a capacity for autonomous growth in near or distant tissues.

Cases 1 and 2 here presented seem to have become irreversible. They
have invaded local and distant tissue, one of them metastasizing. This may
have been a freely transplanted bit of tissue but it had the quality of au-
tonomous growth. In both cases the disease seemed well on its way to de-
stroy the patient within three years of the time when the disease was originally
discovered. It would seem proper then to designate these cases as malignant
and sarcoma instead of "endometriosis" of any type.

Case 3 had the same histologic characteristics as the two previous cases.
Whether all neoplasms with this histologic picture are malignant or not can-
not be stated. The reports in the literature indicate that a considerable pro-
portion have gone on to destroy the patient by a slow progressive infiltration
persisting in some cases for 17 years.

The genesis of this lesion is still debated. Park[11] had the impression from
his examination of the tissue that the disease had a multicentric origin. The
growth of cells from the walls of the vascular spaces certainly suggests this
or even suggests that the neoplasm may have an endothelial origin. How-
ever, this observation will not be accepted until the independence of the
growth from the endometrium is established by serial section. Cullen[12] faced
the same problem before he established the continuity of adenomyosis of the
uterus with the endometrium.

The term sarcoma is employed here to indicate that this is a neoplasm and
not a simple endometriosis. McFarland[13] objects to the use of the word sar-
coma to include so many different types of tumor. He points out that tissues
such as nerve tissue which are found in these tumors are not mesenchymatous
in origin and that the variety of tissue found in the tumors of the urogenital
system suggests a common embryonal genesis. He suggests the use of the
term *dysontogenetic tumor* after Schwalbe. This implies that these tumors are
proliferations of accidentally displaced embryonal fragments. If the em-
bryonal tissue is of a single cell type, then so will the tumor be simple in com-
position. If, on the other hand, the embryonal fragment is composed of sev-
eral types of cell, the tumor will be of the mixed-cell variety.

He found among 475 articles 119 terms applied to the tumors in this re-
gion. If the term dysontogenetic tumor is accepted, it would furnish a con-
venient category into which these three types of tumor here presented might
be placed.

The treatment of this lesion has been surgical. The appearance of the
tissue would place it among the growths which are not susceptible to radia-
tion. We were therefore very much surprised at the apparent susceptibility
to radiation. Massive infiltration of the pelvis and in one case of the ab-
dominal retroperitoneal tissue disappeared completely and have not reap-
peared in 8 and 11 years, respectively.

In the literature there is considerable variability in the reports. Goodall,[14]
in 1944, observed a marked early sensitivity to be followed years later by a
recurrence of the pelvic mass. Park, reviewing published cases, finds that
hysterectomy without radiation has had about the same results as hysterec-

tomy followed by external radiation, but mustered only 16 cases. Henderson,[15] reported a case in which there was residual tumor following hysterectomy. Although no postoperative x-ray therapy was used, the patient was alive six years later.

The technique of x-ray therapy is also irregularly reported. Our own experience in Case 1 may be of interest. She was a member of our staff. A hopeless prognosis was made from the microscopic sections. This was concurred in by Robert Meyer who was visiting us at the time. The patient was 32 years of age. It was decided to let her live her remaining days without the added discomfort of the radiotherapeutic menopause. When the recurrence in the pelvis created an emergency, it was treated palliatively and only when the dramatic recession revealed its sensitiveness to radiation, was it heavily irradiated. Again, at the time when the colostomy was closed, there still remained a palpable mass extending to the region of the left kidney. This was again heavily irradiated.

Similarly, in Case 2, had it not been for our experience with the previous case, we would not have attempted radiation therapy at all because of the extensiveness of the involvement.

It would appear that recurrence of this condition should be treated by radiation, and that radiation should be given to patients in whom there is any doubt as to the completeness of the removal of the tumor. Even if the tumor recurs after seventeen years, there will have been good palliation.

In Case 4 the tumor was limited entirely to the endometrium. There was a greater lack of differentiation than in the preceding cases. The cells did not take the same deep hematoxylin stain as those of the other endometrial tumors. The piece of cartilage, if it was true cartilage and not a simple metaplasia, would place this tumor in the group of teratomas.

Case 5, a case of so-called carcinosarcoma, is presented to illustrate the possibility of there being a reversible stage of neoplasia. The histologic picture of the stromal portion of the tumor showed all the criteria of malignancy yet it did not metastasize with the carcinoma to the vagina. The tumor should possibly be called an adenocarcinoma of the endometrium with stromal hyperplasia. We have seen six of these cases which will be reported in detail later. In four the metastases were pure adenocarcinoma, in one what seemed to be pure sarcoma extending up into the abdomen as a pure adenocarcinoma. The last case appeared in the operative specimen to be pure adenocarcinoma but recurred in the vaginal vault as a mixed-cell sarcoma.

Summary

Three cases of tumor of the endometrium are reported which fulfill the criteria of malignancy. Two of them had massive recurrence after operation and one metastasized. They deserve the term "sarcoma" rather than endometriosis.

They were peculiarly sensitive to radiation.

One case of sarcoma of the endometrium is reported which had a histologic picture unlike that of the two previous cases and contained cartilage. This should probably be called a teratoma, or mixed-cell type of tumor.

One case of so-called carcinosarcoma of the endometrium is reported. This tumor metastasized to the vagina as a true adenocarcinoma suggesting that the sarcoma-like tissue of the stroma was not malignant.

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Discussion

DR. RALPH A. REIS, Chicago, Ill.—The fifth tumor reported is described as a "so-called carcinosarcoma of the endometrium which metastasized to the vagina as a true adeno-carcinoma suggesting that the sarcoma-like tissue of the stroma was not malignant." Of course there is the possibility that this patient had a stromal sarcoma or endometriosis associated with adenocarcinoma. Such a stromal tumor could have disappeared following hysterectomy and irradiation leaving the pure adenocarcinoma found subsequently in the vagina. It is conceded that carcinosarcoma can occur but close study of reports of these tumors shows them to be exceedingly rare. Novak believes that the majority of so-called carcinosarcomas are adenocarcinomas of a very infiltrating type in which the carcinoma cells infiltrate the stroma and simulate an associated sarcoma. Corroboration of this view is found in a report by Saphir and Vass of the Department of Pathology, Michael Reese Hospital. After reviewing the 153 carcinosarcomas in the literature up to 1938, they felt that only 3 were possibly diagnosed correctly and that 150 were diagnosed incorrectly. This group included 36 such tumors of the uterus. In each instance, the resulting metastases of these tumors of the uterus were either simple sarcoma or simple carcinoma, no mixed metastases being found.

It must be borne in mind that errors in diagnosis can arise as the result of (1) variations in carcinoma cells; for example, a squamous-cell carcinoma can have transitional-cell features; (2) marked anaplasia of carcinoma cells; (3) associated inflammation; and last (4) invasion of a benign connective-tissue tumor by a carcinoma or, conversely, invasion of an epithelial tumor by a sarcoma.

The fourth tumor is a mixed-cell tumor, i.e., a teratoma as described by the essayist. Morphologically it is a typical malignancy—a true sarcoma of a type which, in the opinion of our Tumor Clinic, is only slightly more radiosensitive than an adenocarcinoma of the endometrium. Our treatment, like that of the essayist, is surgical removal.

The first three tumors appear to be typical neoplasms of the endometrial stroma. While such tumors occur relatively infrequently, there have been a sufficient number studied in recent years to develop a working knowledge of their characteristics, if not of their origin or of their mode of extension. All three tumors were apparently the result of overgrowth of the endometrial stroma. Such tumors have been described under various names but the majority will agree with Goodall who called them "stromal endometriosis," and described them as being most frequently benign and also radiosensitive. The cells of these tumors do re-

semble those of endometrial stroma but they do not seem to have the characteristics usually associated with malignancy, except for their unusual location. The cells appear regular, there is no invasion, no lawless growth, no anaplasia, no anisocytosis, no poikilocytosis, no necrosis, no hyperchromatic nuclei, and relatively few mitotic figures. There is no invasion of lymph or blood vessels or vessel walls, although they seem to "grow" within the lumen of lymph channels. An aneurysm or a brain tumor may kill a patient by crowding a confined space but these are not truly malignant except in action. Death may occur by surrounding and compressing vital organs; but it would seem desirable to reserve the term malignant for the characteristic microscopic picture with which we are all familiar. There is, therefore, much evidence in favor of calling these tumors "dysontogenetic tumors" as the essayist suggests rather than "endometrial sarcoma."

It is unfortunate that the clinical picture of these three patients could not have been completed. A follow-up on Case 3, a biopsy on the recurrent tumor of Case 2 and a biopsy at the second laparotomy of Case 1, together with an autopsy, might have yielded more and necessary information to round out completely our knowledge of this most interesting endometrial neoplasm.

DR. WALTER T. DANNREUTHER, New York, N. Y.—Dr. Corscaden's paper and included case reports suggest for consideration several interesting questions. First, does a sarcoma really develop on the endometrium primarily? Second, is an endometrial sarcoma less predisposed to remote hematogenous metastases than other sarcomas? Third, is an endometrial sarcoma more radiosensitive than others? And fourth, in cases of carcinosarcoma is it possible to determine whether they coexist incidentally or whether one is secondary to the other?

Dr. Corscaden's first case demonstrates nests of endometrial stromal cells which have apparently undergone malignant transformation, and all the evidence seems to point to the mucosal origin of the tumor. Virchow described and made a distinction between mural sarcome and sarcoma of the mucosa as early as 1864. The structure of sarcomas may vary considerably and large round and spindle cells, decidua-like cells, giant cells, and small round cells may all be seen from time to time. The diffuse distribution of some of these endometrial tumors is testimony that they arise from stromal cells. However, some cases considered as endometrial sarcomas probably represent advanced stages of a myosarcoma impinging on the uterine cavity.

A striking feature of the cases reported in the paper is the meager evidence of remote hematogenous metastases. The metastatic involvement of the abdominal wound in the first case may fairly be attributed to operative implantation, since the patient had a supravaginal hysterectomy, and even the massive retroperitoneal extension may have progressed upward from the cervical stump, just as the recurrence apparently developed by continuity of tissue in the pelvic cavity. The tendency of sarcoma to grow upon a network of blood vessels explains the early invasion of these vessels, while the bulk of the growth accounts for its failure to invade lymphatics. In none of the five cases described in the paper is there any mention of the lungs, which are the most common site of sarcomatous metastasis.

One must agree that the neoplastic tissue in the first two cases showed a remarkable response to roentgen ray therapy, but it is not easy to understand why endometrial sarcoma should be any more susceptible than sarcoma elsewhere. As a matter of fact, no roentgen ray therapy was given in the third and fourth cases, and radium was used in the fifth. All of us have had occasional cases of histologically highly malignant tumors, or patients with an advanced stage of malignant disease, or multiple malignancies in the same patient, which have surprised us by responding dramatically to surgery or irradiation with suvival for many years. Such cases can presently best be explained by some unknown inherent biological factor which endows the individual with something which, for want of a better name, might be called cancer resistance. I recall a patient who continued to bleed immediately after a supracervical hysterectomy at another hospital about ten years ago. I found a definite round tumor in the stump, and took some cytology smears, from which Dr. Locke L. Mackenzie made a preoperative diagnosis of sarcoma, which was confirmed by the pathological report on the

excised tumor. The vaginal vault was treated with radium and the patient is still alive and well. Except in this one case, neither roentgen ray nor radium therapy has seemed to be of much value in sarcoma of the uterus in my personal experience.

The fifth case presented a sarcomatous intrauterine mass, with sarcoma-like stroma intermingled with adenocarcinoma at its base, and subsequent carcinomatous metastasis which showed no evidence of sarcoma. While this may represent a reversible stage of neoplasia, it is also possible that there was such profuse cell infiltration of the stroma that it simulated a sarcoma. Ewing regarded such specimens as unfavorable material for accurate observations on histogenesis.

Dr. Corscaden has presented an enlightening paper and I hope that further experience will justify his optimism regarding the efficiency of heavy roentgen ray therapy in the treatment of sarcoma of the uterus.

DR. EMIL NOVAK, Baltimore, Md.—This paper includes a discussion of several separate and distinct entities. Dr. Corscaden's first case is presumably one of sarcoma, probably of endometrial origin, although the slide shown does not establish the source very clearly, since no continuity of the sarcomatous growth with the endometrial stroma is shown. The essayist has also commented upon the lesion spoken of as stromal adenomyosis or benign stromatosis, which is essentially an adenomyosis in which the invading tissue is made up only of stromal cells, with no gland elements. This invasiveness is at times quite massive, and in at least some cases shows a tendency to intravascular or intralymphatic penetration, even in the absence of any histologic evidence of anaplastic cell activity. The malignant prototype is sometimes spoken of as malignant stromatosis, but why it should be given a special name of this sort I cannot conceive. It is really an endometrial sarcoma, a type of uterine sarcoma which has long been recognized, and it should so be called.

The author's second case is obviously, as he says, of so-called mesodermal mixed type, while the third brings up the question of so-called carcinosarcoma. While I believe that a combination of carcinoma and sarcoma can exist in the same uterus, it is also my belief, as Dr. Reis has kindly quoted me, that the majority of cases in which this diagnosis has been made have been instances of adenocarcinoma. While the latter lesion often shows little or no microscopic evidence of penetration of the basement membrane and invasion of the stroma and musculature, a minority of cases, usually of advanced stage, show pronounced invasiveness of this sort, the infiltrating epithelial cells undergoing degenerative morphological changes which simulate sarcoma perfectly. A meticulous microscope study will reveal all transitions of these changes, and the co-existence of two separate neoplastic types should not be assumed unless such a comprehensive study is made.

DR. CORSCADEN (Closing).—I meant to anticipate the disclosure of the Achilles' heel of those two first cases reported; that is, the lack of biopsy and simply relying on the original specimen. For the purpose of the report, those should be included.

I am glad that Dr. Novak stressed the importance of not trying to express malignancy in terms of black and white. Normal pregnancy has anaplastic cells that invade and in all of the cases chorionic tissue metastasizes but malignant mole is excessively rare. Carcinoma of the cervix we now speak of as metaplasia, basal cell, hyperplasia, cancer in situ, early invasive, etc. There is a gradation in most of these diseases, at least there are samples which form a gradation from the perfectly benign to the absolutely malignant.

THE BEHAVIOR OF PSEUDOMUCINOUS CYSTADENOMA*

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PFANNENSTIEL,[1] believing that the surgeon should have a descriptive name for the cystadenomas, suggested pseudomucinous and serous as terms portraying the cyst contents of the two ovarian tumors whose outward appearances are so much alike. It was following this clarification that the pseudomucinous cystadenoma of the ovary became a distinct clinical and pathological entity. There has followed, however, a growing literature with relatively few statistics from which to draw conclusions. This has led to confusion regarding incidence, histogenesis, and benign or malignant spread. A review of the literature coupled with our experience leads me to believe that the pseudomucinous cyst is not as common as it is usually thought.

Incidence

In order to make an appraisal of our own incidence of pseudomucinous cystadenoma we have first determined the frequency of ovarian cystectomy for benign and malignant primary tumors. The total private and ward admissions to the gynecology service at Temple University Hospital for three years (1947, 1948, 1949) were 3,598. Of this number only 67, or 1.86 per cent, had neoplastic ovarian disease necessitating surgery. To further check this figure, we took 2,000 consecutive private admissions to our service and found 47, or 2.35 per cent, ovarian tumors. It is obvious that ovarian neoplasia constitutes a small fraction of this gynecologic practice and to obtain material for statistical survey requires a vast amount of material to have validity. In the past ten years our department of pathology lists 332 primary ovarian tumor specimens. The bilateral growths are counted as one specimen. Thirty, or 9 per cent, were of the pseudomucinous type and 26, or 7.8 per cent, were serous. The most frequent benign ovarian tumor encountered was the dermoid, making up 71 cases for an incidence of 21.3 per cent.

Reviewing the literature I find discrepancies in the incidence figures to the point of confusion. Goodall[2] states, "Pseudomucinous cysts constitute the great majority of ovarian cystomata," and Hertzler[3] claims an incidence of 50 to 75 per cent of all cystomas that come to operation. These statements have found support in the writings of Rankin and Donald,[4] Wilson and Sims,[5] while Weiner,[6] one of the early writers in this country, stated that pseudomucinous tumors constituted two-thirds of all ovarian growths. Pathology texts, Bell,[7] Smith and Gault,[8] and Novak,[9] give an equal distribution to pseudomucinous and serous cysts and feel that together these two varieties constitute the most common ovarian neoplasms.

Allan and Hertig,[27] analyzing all cases of primary ovarian tumors over a 43-year period, found 1,740 cases. Of these 21 per cent were pseudomucinous. Such a marked difference in our figure and that of Allan and Hertig indicates the necessity of a large series, and further the length of time required to build a statistically significant set of figures.

Mayer[10] found an incidence of 0.21 per cent pseudomucinous cysts among his gynecologic cases. Following Mayer's method of calculation we find ourselves with an incidence of 0.25 per cent, using surgical admissions only for calculation. These two figures compare favorably with Miller's[11] collected statistics from several hospitals relative to the pathology encountered where oophorectomy had been done. He found one pseudomucinous cyst in 461 so-called small ovarian tumors (0.21 per cent).

Although there is a discrepancy in the related figures on incidence, I feel that we can accept only those based on a large series such as reported by Allan and Hertig. It would seem that pelvic laparotomy for ovarian neoplasia should be a rather uncommon operation and specifically for pseudomucinous cysts.

Histogenesis

Hertzler[3] stated that we possessed little understanding of the pseudomucinous cyst since it was not discovered until considerable growth had taken place and it had developed in a characteristic fashion. MacCarty[12] in a paper published in 1913 considered the tumor to arise from hyperplasia of the lining epithelium of simple cysts or the "stratum germinativum" of the ovary, while Goodall[13] stated that pseudomucinous cysts were ovulogenic and also came from germinal epithelium. Reagan[14] claimed that Gardner in 1932 "probably was the first to demonstrate" the origin of this tumor from follicular epithelium.

Many writers on this subject have pointed out the striking similarity between the tumor and the glandular arrangement of large bowel. Thus some investigators class pseudomucinous cysts as teratomas in which the innermost somatic layer (entoderm) alone is reproduced. R. Meyer[15] was the first to feel that "columnar entodermic epithelium supplanted other teratomatous elements." Mueller[16] likewise has made this claim.

The author, while performing a hysterectomy, found what appeared grossly to be a very small pseudomucinous cystoma. This cyst (about 2 cm.) resembled the usual follicle cyst. It seemed to have little epithelial covering and had a slightly dirty gray color. Upon incision an adhesive mucinaginous material appeared that would not be sponged away. It was hoped the histologic study might provide some further evidence on histogenesis.

Histologic study by Dr. W. N. Campbell of our pathology department follows: "Sections through the ovary reveal a corpus luteum and, in one small area, a short fragment of tall cylindrical epithelium of picket fence type covers one portion of the ovary. This is definite enough to suggest a diagnosis of pseudomucinous cyst. The origin of this structure cannot be determined. The remaining portion of the ovary was searched carefully for evidence of a Brenner tumor but none was found."

Pathology and Clinical Behavior

The histologic characteristics of the pseudomucinous cystadenoma hardly need reviewing. The occurrence of dermoid cysts in or associated with the pseudomucinous variety is a well-documented point as shown by Foote,[17] and Wilson and Sims.[5] In our series of 30 cases, one of these tumors was found to "arise from a Brenner tumor" and another case revealed a small dermoid in the cyst wall.
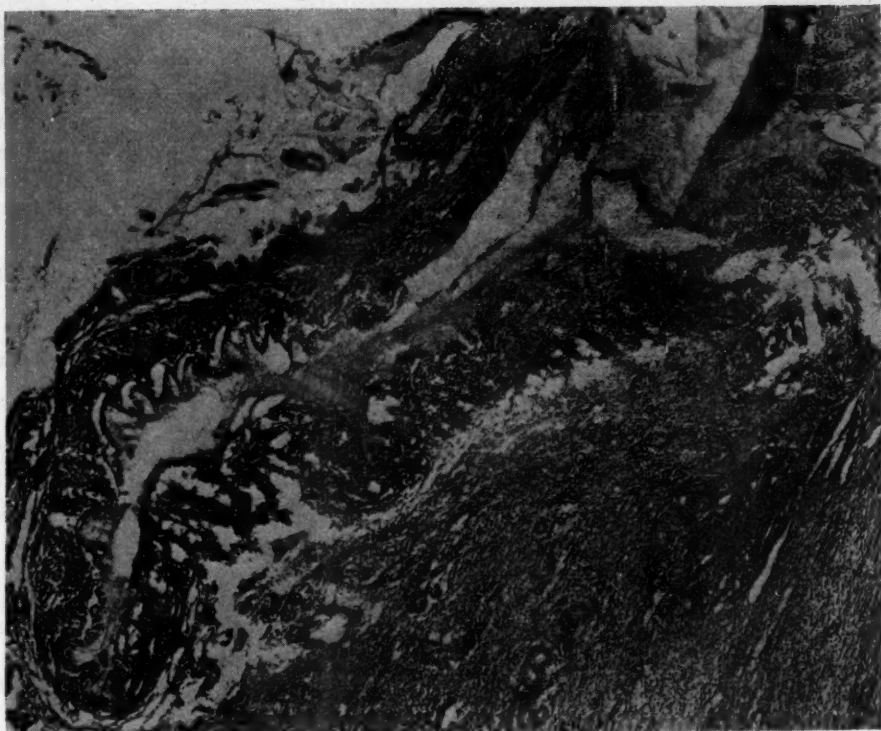
Fig. 1.—No. 62319. Small pseudomucinous cyst. (×50.)

Fig. 2.—No. 62319. Small pseudomucinous cyst. (×200.)

Masson and Hamrich[18] and Calkins and True,[19] as well as textbooks of gynecology, indicate that pseudomyxoma peritonei is commonly associated with pseudomucinous cysts. We found no instances of this in our series.

Since the first report of ovarian fibroma and associated hydrothorax (Meigs' syndrome) there have been several case reports of the same syndrome occurring with pseudomucinous cystadenoma (MacFee[20]; Nora and Davidson[21]; Millett and Shell[22]; Rosenfeld[23]). This was not discovered in any of our 30 cases.

Novak[9] quotes Meyer's collected statistics as denoting a 5 per cent malignant degeneration occurring in this tumor, whereas Goodall[2] states that malignancy is a very common change in pseudomucinous cysts. In the 332 cases of ovarian tumors reviewed, we could find only two such cases, one of which will be recorded here; for fifteen months we questioned whether this (to be documented) was a true malignancy.

From these several documented points, there is a striking disparity of thought and experience concerning the clinical behavior of this tumor. It is our impression that the pseudomucinous cystadenoma is an unusual growth possessing a very bizarre and unpredictable clinical pattern.

Weiner[6] reported a case wherein the histology was benign but destruction of the cervix occurred along with pulmonary metastases. All tissue at autopsy as well as from the original operation was benign on histologic study. He did not agree with Pfannenstiel's statement that metastases were by implantation only. Both Weiner and Baumgarten[24] report having seen benign cystadenomas metastasize along blood and lymph channels.

An excellent report of the behavior of this tumor is presented by Brandberg[25]: "The condition of metastases in benign ovarian cystomata are among the most interesting and unique problems relating to these tumors." He stated that metastasis along blood and lymph vessels takes place in exceptional cases. He reported a case wherein metastases to the spleen occurred 25 years after he had removed a bilateral pseudomucinous tumor. Schultze-Henbach[26] reports an identical case of splenic metastases 15 years following removal of the primary. In both reports the histology of the primary and the secondary growths was benign and identical.

The following case illustrates several unusual features of this tumor while covering a period of 10 years.

CASE 1.—Mrs. C. F. (No. 20-49-2006), aged 55 years, first consulted me on Jan. 21, 1949. She stated that she had felt a mass in the lower abdomen for the past nine years. In the past five months this mass had increased in size so that she was uncomfortable for the first time. In addition, she related that an osteopath had been treating an ulcer on the vulva for the past four years. Menopause was complete eight years previously and there had been only occasional "spotting" following trauma. Examination revealed a multinodular cystic mass extending to the umbilicus. This was movable and not tender. We were uncertain as to free fluid in the abdominal cavity. There were many large lymph nodes felt in both inguinal regions extending down both femoral triangles. Arising in the fossa navicularis and extending into the vagina was a granular, proliferative, slightly movable mass about 3 by 4 cm. This area bled slightly upon examination. The pelvic cavity was filled with a large cystic mass.

Presumptive Diagnosis.—Double primary pelvic lesions, i.e., carcinoma of the ovary and carcinoma of the vulva with metastases to the inguinal and femoral nodes.

Procedure.—An abdominal exploratory operation was done first to ascertain the extent of the pelvic lesion before considering the vulvar pathology. At operation we found bilateral ovarian cystomas measuring 35 cm. There was no gross evidence of malignancy. A pan-

hysterectomy with bilateral salpingo-ovarian cystectomy was done. This procedure allowed us to proceed at once to a complete retroperitoneal lymph node dissection. Our thought in so doing was concern over the spread to this region from the vulvar growth. One large node

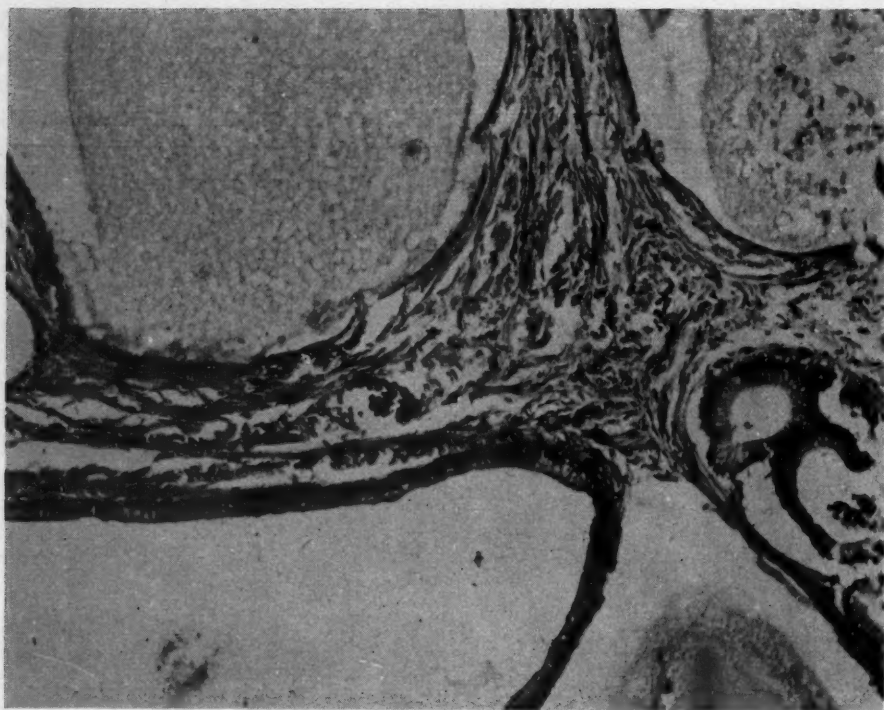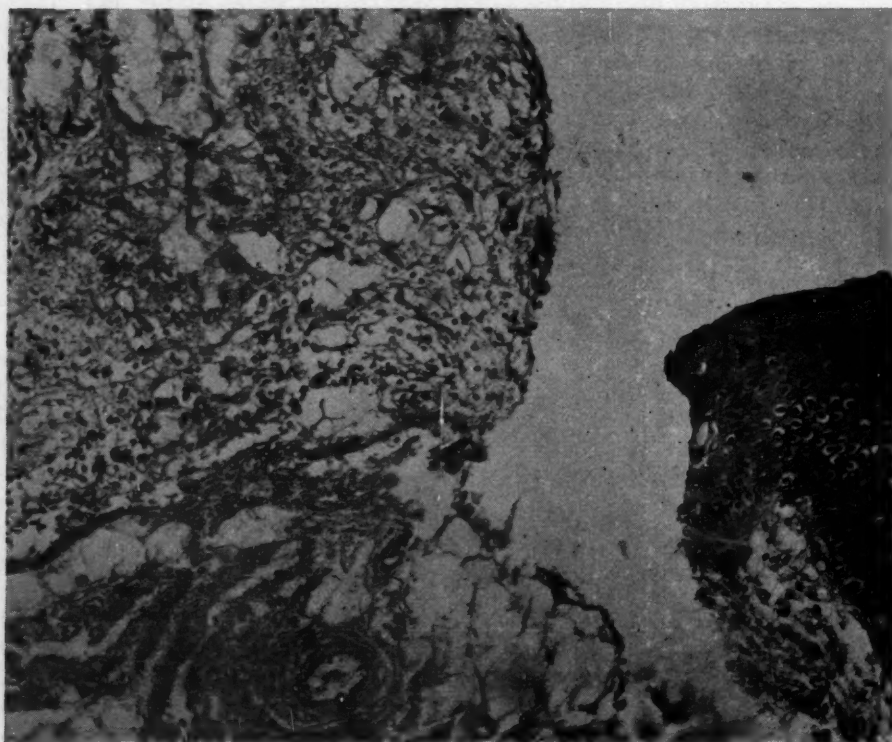Fig. 3.—Bilateral ovarian cystomas.

Fig. 4.—Metastases to the vulva.

(4 cm.) was removed from the left obturator fossa and the remaining lymphatics removed appeared to be normal. Before the patient left the operating table, we obtained a large biopsy of the vulvovaginal lesion.
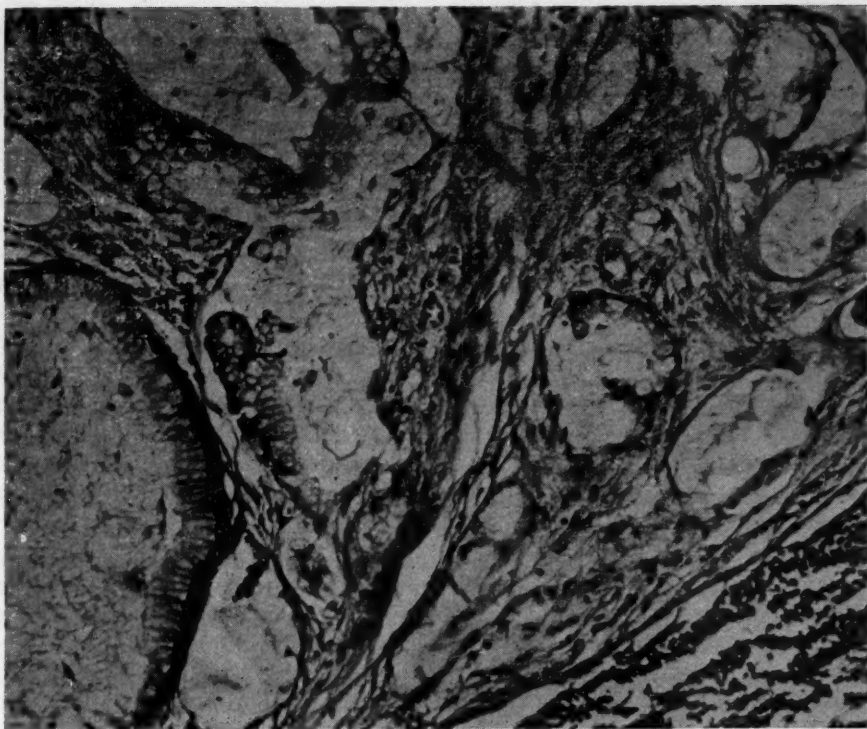
Fig. 5.—Ovary.   (×180.)

Fig. 6.—Vulva.   (×180.)

Fig. 7.—Lymph node. (×180.)

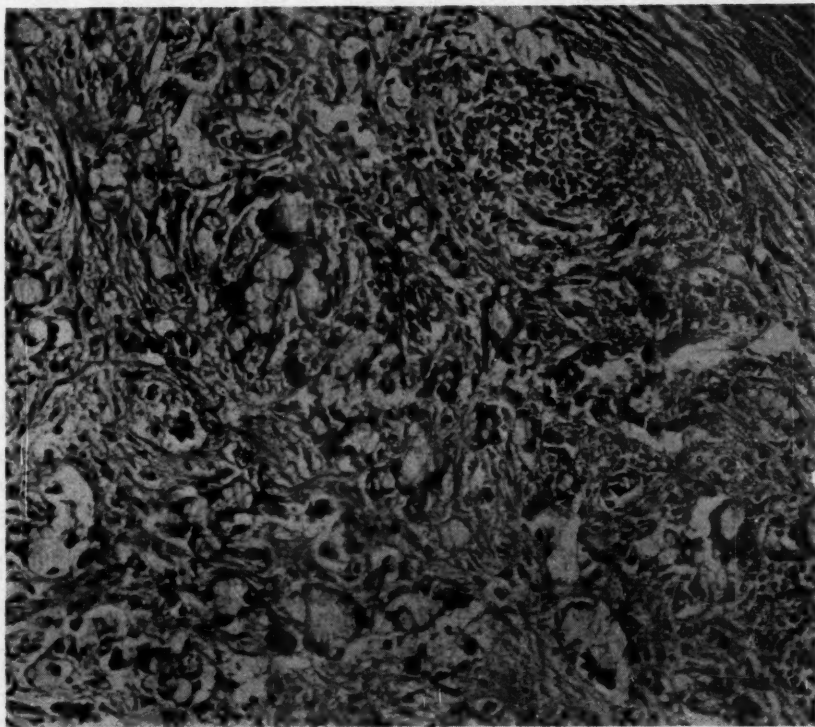
Fig. 8.—Vaginal recurrence. (×200.)

Pathological Diagnosis.—Pseudomucinous cystadenocarcinoma with metastases to the retroperitoneal (obturator) lymph node and the vulva. Numerous tissue sections were examined, and the cellular pattern was found to be benign in all the specimens. The diagnosis of malignancy was based on the metastases to the lymph node and to the vulva.

One week after the abdominal procedure, a radical vulvectomy and bilateral inguinal and femoral lymph node dissection were performed. The vulvar lesion and the lymph nodes presented the same benign histologic pattern as noted previously by the pathologist (Figs. 5, 6, and 7).

This patient was followed at intervals of one month for one year after the operation. Fifteen months following surgery at the regular visit we discovered evidence of recurrence immediately under the vaginal epithelium about 4 cm. in from the perineum. There were two small nodules of about 2 cm. at "7 and 5 o'clock." The two recurrences were excised widely so that the entire posterior vaginal wall and rectovaginal septum were removed.

The tissue study on this specimen was quite different from that encountered during the previous surgery. Dr. A. R. Peale of our pathology department reported: Metastatic adenocarcinoma, mucoid or pseudomucinous type (Fig. 8).

Comment

We have found little uniformity in the literature concerning pseudomucinous cystadenomas. Our small series of primary ovarian tumors reveals a 9 per cent incidence of this neoplasm. Our figure is similar to some of the reports on incidence.

The most striking observation both from the literature and our case report demonstrates a tumor unparalleled in dissemination. Until we encountered the recurrence with a different cellular pattern we thought we were dealing with an instance of a benign metastasizing tumor. One cannot help but speculate that further recurrences may demonstrate some modification of the most recent histology.

We appreciate the work of Mrs. Elsie G. Seyffert and Dr. W. R. Penman in supplying us with certain figures for this study. We are grateful for suggestions from Dr. J. Robert Wilson.

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Discussion

DR. LUCIEN LeDOUX, New Orleans, La.—In selecting this subject, Dr. Beecham has chosen one that is not only very interesting, but from his review of the literature and from his own experiences it is one that has several controversial aspects.

These cysts, as has been pointed out, have as one of their characteristics a mucinlike content, which after cooling becomes semisolid, hence it is called, ''pseudomucinous.'' If the protein content of the ''fluid'' is high the material may solidify. Further study of this material may prove interesting. I was particularly interested in what Dr. Beecham had to say regarding the incidence of cystadenomas, especially as his figures parallel to some extent the figures I wish to quote you which, while not large, are nevertheless interesting:

A review of 1,709 consecutive gynecological admissions at the Hotel Dieu during 1947-1948 revealed the following incidence of these tumors: Pseudomucinous cystadenoma 12, pseudomucinous cystadenocarcinoma 0, serous cystadenoma 11, serous cystadenocarcinoma 2, dermoid cysts 9. These figures reflect an equal distribution of the serous and pseudomucinous cysts, a fact which is mentioned in the pathology texts of Novak and others.

Furthermore, it appears that a 0.65 per cent incidence in the 1,709 cases of the Hotel Dieu series is fairly in balance with the 1.86 per cent in 3,598 cases of the Temple series, though somewhat under the 2.35 per cent in the 2,000 cases of Dr. Beecham's private series. The percentage which I quoted is probably more in keeping with the figures of Mayer, 0.21 per cent, of Miller, 0.21 per cent, and of Dr. Beecham, 0.25 per cent. Admittedly, more studies of this kind are necessary before we can collect enough material to make our figures sufficiently impressive as to be conclusive.

It is also interesting to note that none of the cases in the series I mentioned were complicated by either Meigs' syndrome, ascites, or transplantation or metastases to the large intestine, any of which it is known may occur.

In a very comprehensive and well-documented case report, the essayist draws our attention to an instance of metastatic pseudomucinous adenocarcinoma. This very malignant picture, fortunately, rarely occurs in the pseudomucinous group. Available studies to date seem to indicate that the incidence of pseudomucinous cyst is low and the occurrence of the malignant type through metastasis is rare.

DR. C. L. RANDALL, Buffalo, N. Y.—I appreciate the opportunity to discuss Dr. Beecham's paper. Pseudomucinous cystomas occur frequently and often present several problems. I cannot evaluate the histology reported but we have been following the clinical course of patients after removal of cystadenomas of the ovary.

Reviewing 1,300 ovarian tumors at the Buffalo General Hospital, we recently found that nearly 14 per cent were cystadenomas considered benign, and of 179 such tumors, 95 were serous cysts while 84 had a pseudomucinous content. Since 16 per cent of our ovarian neoplasms were malignant and 12 per cent were dermoid cysts, we might expect to encounter a pseudomucinous cystoma half as often as dermoids or primary ovarian malignancies.

Most of us are at times uncertain as to the malignant potentiality, not only of the rarer ovarian tumors, but of some of the more commonly observed cystomas as well. If the lining of a cyst appears grossly papillary, whether the fluid content is serous or pseudomucinous, is there not a chance that the tumor will ultimately prove to be malignant, even though the sections show it to be histologically benign? This is certainly the case when pseudomyxoma peritonei gives rise to progressively extending adhesions and, ultimately, death from

intestinal obstruction. However, we have found this danger to be more apparent than real. During the 12-year period surveyed only one case is known to have occurred among 84 patients observed after removal of a pseudomucinous cyst.

A second problem is evidenced by the suggestion that whenever a cystoma is removed the chance of a similar tumor subsequently developing in the opposite ovary indicates bilateral oophorectomy. This was done in 7 of our cases and none of the women so treated have reported further trouble. However, after preservation of the uninvolved ovary we have followed 58 patients, 33 for periods longer than 5 years, 17 for longer than 8 years, during which time only one of the 58 women, after 4½ years, developed a similar pseudomucinous cystoma in the remaining ovary. Should a unilateral cystoma prove to be of the serous type, our figures suggest at least a 4 per cent chance that the remaining ovary will develop a pathologic condition requiring another laparotomy. On the other hand, if the cystoma is pseudomucinous there appears to be considerably less indication for prophylactic removal of an uninvolved apparently normal ovary.

There is some cause for concern when a large cystoma has been reported to show no malignancy for fear the sections missed a malignant area. This brings up the question, does the discovery of a papillary lining imply a probability of further trouble? If there were no implants outside the capsule we have observed no recurrence of neoplasm in 16 women followed with one ovary preserved after removal of a cystoma showing a grossly papillary lining. In the one patient developing pseudomyxoma peritonei to date, papillary implantation outside the cyst wall was evident at the time of laparotomy. We have been unable to follow two cases but of the 13 others being observed, 6 for more than 5 years, no others have shown evidence of recurrent disease. In three cases both ovaries were removed because of papillary cystomas replacing both ovaries, but neither of the two that have been followed more than four years have to date developed evidence of recurrent tumor.

While the gross picture seems to be of significance, in our material the histologic evaluation appears more important. If at operation the picture suggested malignancy, with papillary implantation on adjacent peritoneal surfaces, yet the pathologist reported the tumor histologically benign, the subsequent clinical course has agreed with the histologic prognosis. During this 12-year period the same pathologist reported 214 tumors of the ovary as unquestionably malignant. One-half of the patients were dead within six months after their ovarian carcinoma was discovered. Among 134 operated upon prior to 1945, the incidence of 5-year survivals approximates 15 per cent. Though only routine sectioning and ordinary staining were done, we are inclined to conclude that the histologic picture usually provides a reliable basis upon which to estimate the prognosis.

I am grateful to Dr. Beecham for calling our attention to a most interesting, but, I believe, very rare behavior for pseudomucinous cystomas of the ovary.

DR. EMIL NOVAK, Baltimore, Md.—Dr. Beecham spent considerable time in discussing the relative incidence of pseudomucinous and serous cystadenomas, and the figures of the various authors which he has quoted show considerable disparity. I am frank to say that I have never been much excited about the fact that in some series there is a moderate preponderance of one type, in other reports, of the other, but they seem on the whole to be fairly evenly divided.

The particular point of the paper is the demonstration of a primary pseudomucinous cystadenoma which, from the sections here shown, is unquestionably histologically benign, with other sections of metastases which are just as unquestionably malignant. The natural conclusion in a case of this sort, as I wrote to Dr. Beecham when he kindly sent me sections of this material, must be that somewhere in the original tumor there must have been cells which had undergone malignant transformation, even though these were not discovered after many blocks were made. While one can conceive of the remote possibility of transportation of benign elements, one would in this case also have to postulate later malignant changes in multiple foci, and this would be very far fetched indeed. The probabilities, therefore would

seem to be that actually malignant cells were present somewhere in the original tumor, although the route of dissemination was different from that seen in most pseudomucinous cystadenocarcinomas.

DR. A. D. CAMPBELL, Montreal, Quebec.—This is a very interesting subject. It is rather difficult, however, to classify ovarian cysts on the operating table, and still more difficult preoperatively.

The pathological aspect of these tumors is of more than academic interest and one should always bear in mind the high incidence of malignancy in them. Donald McIntyre of Glasgow, some years ago in reviewing some 700 to 800 cases of ovarian tumors, found the incidence of malignancy to be in the neighborhood of 38 per cent. In our Clinic at the Montreal General Hospital, the incident of malignancy was approximately 22 per cent. Such finding makes one feel that all ovarian tumors are potentially malignant. Unfortunately, there is a tendency on the part of too many of our colleagues to minimize the possible dangers of malignancy in ovarian tumors, comforting themselves and the patient that pseudomucinous cysts are relatively benign and for that reason postponing surgery.

For the benefit of our House Officers and as a guide to our own thinking, I have used the following as a sort of yardstick:

1. If a cyst is 5 cm. in diameter, the abdomen should be opened and the cyst removed.

2. That all the pelvic organs should be removed: (a) If cysts are bilateral. (b) If the patient is over 45 years of age but the cyst unilateral. (c) If the tumor on close examination appears to be malignant.

DR. BEECHAM (Closing).—The discussion has revealed some agreement on incidence. As Dr. Novak points out, this is really of academic interest. One point I had hoped would be evident, that this tumor is relatively uncommon, and as Dr. Norman Miller has pointed out on numerous occasions, the ovary continues to be attacked as though ovarian neoplasms are very common. I think Dr. Novak's explanation is probably the correct one, that there were malignant areas missed although a great many sections were taken. This instance is our first encounter with retrograde metastases from ovarian carcinoma.

AN INJECTION STUDY OF THE BLOOD VESSELS OF THE
BLEEDING UTERUS*

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THE clinical management of a patient with functional uterine bleeding is still a discouraging and troublesome problem.

Pathologically, study of the uterus from a functional uterine bleeder is disappointing. By ordinary means, in the vast majority, nothing can be learned as to the cause or mechanics of the bleeding. The type of endometrium, except in a few such as the hyperplasias, has no bearing. Perhaps Otto Schwarz,[1] by his demonstration of unresolved elastic tissue about vessels in the group of subinvolutions, has presented the only concrete pathological change of any use in the laboratory. It would seem that we could look forward to the time when some further classification of these organs from bleeding women can be made and perhaps some useful light thrown thereby on the treatment of this troublesome condition.

Whenever possible during the last few years, the vessels of uteri which had to be removed for functional bleeding were injected with synthetic liquid latex injection compound which is a milklike liquid in its natural state. Naturally, specimens of this type available and suitable for injection are not common. They are not available because hysterectomy is not done for this disorder when it is possible to avoid it, and only after all other means of treatment have failed. Some specimens are not suitable because for proper cannulation of the veins and arteries the uterus has to be removed with the specimen untraumatized. This eliminates almost all specimens from difficult operations.

The technique of injection of the vessels of the uterus is reported in previous papers and need not be repeated here.[2] Suffice it to say that the great advantage of this injection compound is that it is easy to use. It does not require preparation before using except for filtering and may be used on specimens at room temperature. As time has gone on it is obvious too, that it has some limitations as an injection mass. With it the author has not been able generally to fill the spiral arteries of the endometrium in spite of the fact that general arterial injection of the uterus is an easy matter. In other words, it seems to be a rather gross injection material, even under high pressure not permeating fine arterial channels (Fig. 1). All the reasons for this failure

are not apparent. The size of pigment granules used has been checked and found to be small enough but, as in all injection work, other factors such as surface tension and viscosity of the compound have to be taken into consideration.

Perhaps because of the gross qualities of this material, it was decided to continue its use in the injection of bleeding uteri, to get a rather bird's eye view of their vascular differences, if any, from those of uteri with normal vascular control previously injected with the same material and by the same technique.
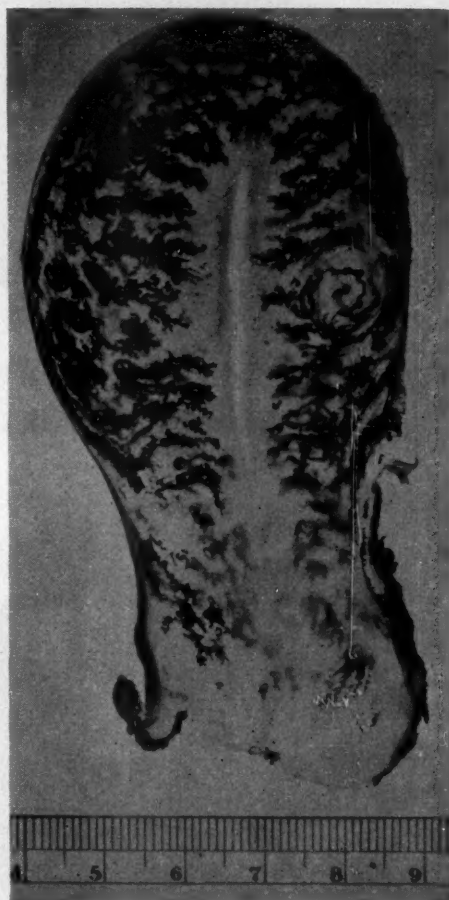
Fig. 1.—Average arterial injection of uterine blood vessels obtained with synthetic liquid latex. (From AM. J. OBST. & GYNEC. 47: 185-197, 1944.)

There is the personal feeling that failure to demonstrate spiral arteries of the endometrium is not a serious matter. They have been studied by experts,[3, 4] and although much has been learned about the phenomenon of menstruation, it is still a phenomenon, and we have very little more understanding of excess bleeding from the uterus than we had one hundred years ago. The fascinating physiology of the uterus as it is now known is well outlined and documented by Reynolds.[5] Shunts or anastomoses between endometrial arteries and veins have been demonstrated by Schlegel.[6]

Injection of the uterine blood vessels with liquid latex demonstrates in best detail the veins of the myometrium and endometrium. The veins of the uterus must not be forgotten as the possible source of at least part of menstrual flow, and nothing is known of the role of venous reflux in abnormal uterine bleeding.

Fig. 2.—Inner myometrium and endometrium of normal uteri do not inject after menstruation.

Fig. 3.—Premenstrually, veins of the endometrium are filled. (From AM. J. OBST. & GYNEC. 49: 1-9, 1945.)

Fig. 4.—During menstruation, venous mass appears in uterine cavity.
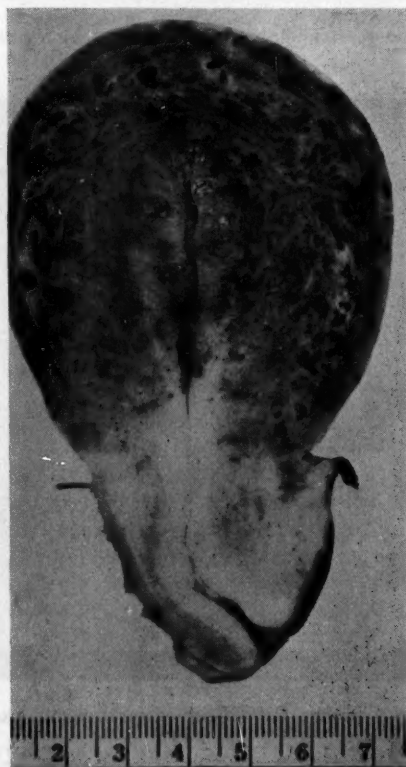
Fig. 5.—Conspicuous sinusoids and leakage into uterine cavity by cycle day 22 in severe hypermenorrhea.

In the uterus with good vascular control, little or no injection of the inner zone of the myometrium is obtained in the days following menstruation (Fig. 2). After ovulation, and progressively to the period, the veins of the
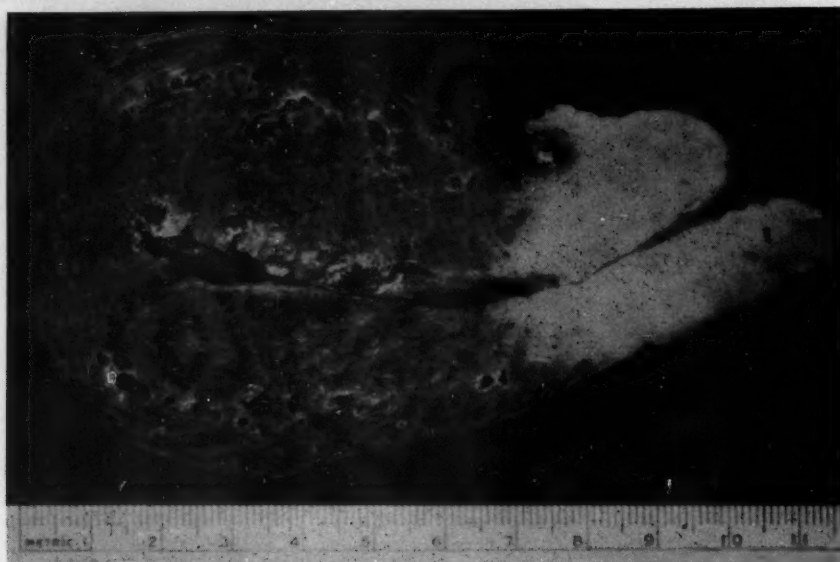
Fig. 6.—Similar sinusoids and leakage into uterine cavity by cycle day 18 in another case of hypermenorrhea.
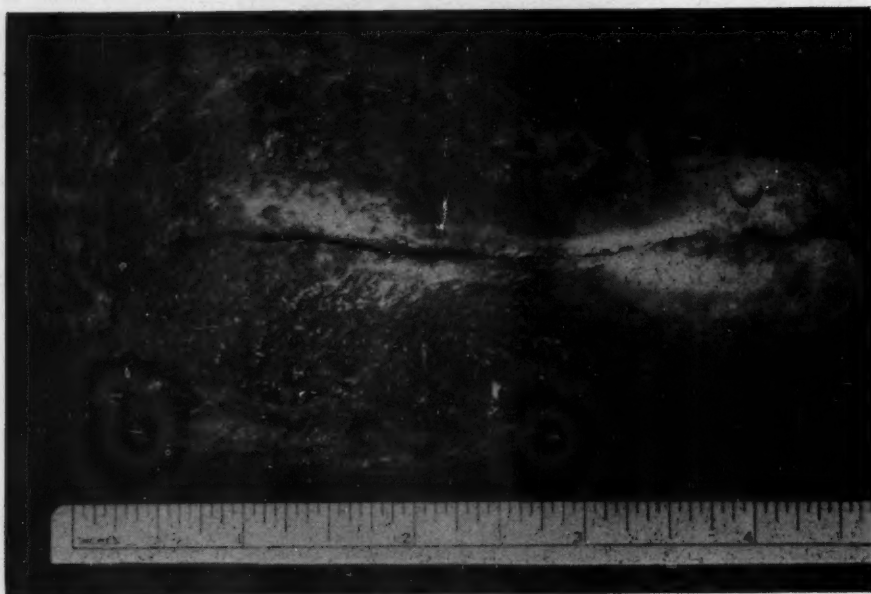
Fig. 7.—A clinically soft, boggy uterus but no hypermenorrhea. Large peripheral veins, but no endometrial sinusoids.

endometrium and surrounding myometrium become easily injectable (Fig. 3). Venous injection mass normally appears in the uterine cavity just before and during menstruation but at no other time (Fig. 4).

When we turn to the uterus with poor vascular control a large group of such uteri show no uniform pattern of injectability except easy permeability of the venous mass to the uterine cavity regardless of the time in the cycle.

Fig. 8.—Hyperplasia of endometrium. No bleeding for two weeks. Patchy venous and arterial injection of endometrium. Arteries at "A" in endometrium.
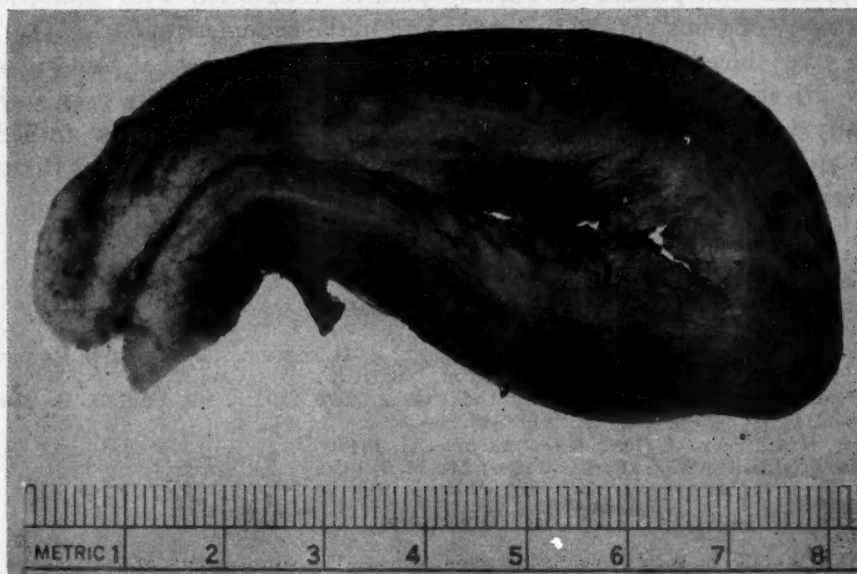
Fig. 9.—Hyperplasia of endometrium, bleeding. Arterial as well as venous channels are injectable in the endometrium.

In uteri from many women with hypermenorrhea, but no intermenstrual bleeding, the venous sinusoids of the myometrium and endometrium become conspicuously filled early in the cycle and there is no orderly delimiting zone in the inner myometrium (Figs. 5 and 6). Injection mass appears in the

uterine cavity in most specimens. The general picture is that of chronic passive congestion in all vessels of the uterus.[7] Occasionally the peripheral veins of the myometrium may be large (the uterus soft and boggy clinically) without large sinusoids in the endometrium. Hypermenorrhea in these patients is not a conspicuous feature (Fig. 7).

In the uterus with hyperplasia of the endometrium, a limited injection experience indicates that venous sinusoids in the endometrium are less conspicuous but that regardless of whether bleeding is going on at the time or not, a patchy injection of the endometrium is possible (Fig. 8). In photographs it may be seen that, as in no other uteri, arteries of the endometrium are injectable in hyperplasia (Fig. 9). This may support the recent view of Schwarz that there is hypertrophy of the arteries in this condition.[8] Perhaps in uteri which bleed by irregular shedding of the endometrium, as is supposed to occur in hyperplasia, the observation of the patchy injectability is not unexpected.

Conclusions

Injection of blood vessels of uteri which bleed irregularly or constantly from nonhyperplastic endometrium show no definite vascular pattern, and nothing else noteworthy, except the ability to force venous injection mass into the uterine cavity at almost any time of the cycle.

Many uteri which exhibit hypermenorrhea, without bleeding at any other time, present the picture of chronic passive congestion with dilatation or hypertrophy of veins both peripherally and in the endometrium.

In uteri bleeding or recently bleeding from endometrial hyperplasia, a patchy injection of veins of the endometrium, and of arteries as well at almost any time is apparent from a limited number of specimens studied. It would appear that in hyperplasia there is hypertrophy, or at least dilatation of arteries in the endometrium.

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Discussion

DR. FRANK E. WHITACRE, Memphis, Tenn.—The spiral artery of the primate endometrium was described by Daron, and its apparent role in menstrual bleeding was contributed by Markee. Okkels and Engle brought out evidence that these and other vessels in the uterus are peculiarly dependent upon ovarian hormones in their morphological and physiological development.

With these data at hand one could construct a logical concept of normal and abnormal uterine bleeding and could be hopeful that a full solution to the problem of functional bleeding was not far off. Our concepts were shaken by the demonstration of Kaiser that some menstruating monkeys get along without spiral arteries.

Dr. Faulkner feels that his failure to demonstrate spiral arteries in the endometrium is not a serious matter. This disturbance of current concepts does not mean that numerous findings concerning the uterine blood vessels are wrong. It rather emphasizes that the use of these facts in the construction of hypotheses is mistaken or incomplete. In the work just presented it was found that the injection mass reached the uterine lumen in most instances, which may indicate that the walls of the vascular channels were interrupted or seriously weakened. This is a normal occurrence during the period of endometrial regression which precedes menstruation and is due to hormonal changes. The altered condition of the blood vessels leads to hemostasis and edema. It would be remarkable if the uterus were able to withstand the effect of degenerative by-products, protein in nature. According to Markee this leads to vasoconstriction of the spiral arteries and dilatation of the veins. As stasis occurs so does disintegration of the vascular architecture, resulting in more or less profuse bleeding.

The essayist has pointed out that functional uterine bleeding may occur at any phase of the cycle from an endometrium of variable morphology. What part euglobulin or menstrual toxin may play in affecting vascular destruction is not clear. Also the role of estrogen in producing endometrial proliferation and marked vascular response is not well understood. One cannot escape the conclusion that studies such as the one just reported, together with an examination of the microscopic anatomy of the endometrium and correlated with the patient's bleeding characteristics will be needed to solve this complex problem. Also, there is mounting evidence of the cortical control of the autonomic nervous system, and one is led to suspect that the rich supply of nerve endings to the uterine vessels is probably concerned in this mechanism and must await further investigation.

DR. FAULKNER (Closing).—I would like to thank Dr. Whitacre for his generous remarks and to say that I quite understand why general discussion of a subject of this sort is shied away from. It is a physiologic problem. It is probable that anatomic studies of this kind contribute but little except as to the possible mechanics produced by the physiology, but in the meantime the fooling of ourselves goes on in gynecology. With functional bleeding, we teach and talk one way, and practice another, and I think that some day, and as soon as possible, we should be able to escape and to save ourselves from the disgrace of removing normal uteri, or at least morphologically normal uteri.

ENDOMETRIAL CARCINOMA ASSOCIATED WITH FEMINIZING OVARIAN TUMORS*

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THE increasing interest in the feminizing tumors of the ovary in the last ten years has brought to light a considerable group of cases in which these tumors occurred in combination with carcinoma of the endometrium. The relative frequency of this combination has been interpreted as added evidence of the carcinogenic property of estrogens. The investigation of this "spontaneous biologic experiment in the human being"[1] offers rich opportunity for the study of the role of estrogens in the development of uterine carcinoma. The purpose of this paper is to collect and examine the reported cases of this combination, to report 4 new cases from our own laboratory, and to evaluate the relationship between postmenopausal production of estrogens, endometrial hyperplasia, and carcinoma of the uterus.

Schroeder[2] in 1922 was the first to report a case of concurrent granulosa-cell tumor and endometrial adenocarcinoma. Both Schroeder and Robert Meyer emphasized the difficulty in distinguishing carcinoma from atypical endometrial hyperplasia in this patient. Today this difficulty still remains the chief pitfall in the study of such cases. For 10 years following Schroeder's report the subject received little attention. The identification of thecoma in 1932 by Löffler and Priesel[3] added impetus to the study of feminizing tumors, and a few scattered reports of these tumors, combined with uterine carcinoma, appeared in the literature. More recently Dockerty,[4, 5, 6] Henderson,[7] Woll and associates,[8] C. B. Ingraham,[9] and others have reported larger groups of this combination.

There is a growing conviction among several investigators (Fischel, Novak, Geist, Traut) that both the thecoma and granulosa cells have their origin in the undifferentiated cells of the ovarian mesenchyme. The luteoma is thought to represent the complete or partial luteinization of the thecoma or granulosa-cell tumor. These elements are frequently found together in the same tumor,[10] and because of their common histogenesis and frequent co-existence the term *feminizing mesenchymoma of the ovary* has been suggested by Novak to include all these tumors. (The term will be used with this meaning in this discussion.) For the sake of brevity, the combination of feminizing tumor of the ovary and carcinoma of the uterus will frequently be referred to as the "combined tumors."

Survey of Reported Cases

The literature from 1920 through 1949 has been reviewed. An attempt was made to evaluate the diagnosis, particularly that of endometrial carcinoma, in each reported case. Photomicrographs and verbal descriptions of the slides

were reviewed carefully. Only those which fulfilled at least the minimal criteria of carcinoma were included. In some cases the diagnoses of competent gynecological pathologists were accepted in the absence of photomicrographs or detailed descriptions of the slides. We realize that in some cases the diagnosis of what is carcinoma and what is atypical endometrial hyperplasia will vary among a group of the most skilled pathologists, and we are fully conscious of our own vulnerability in this appraisal of cases reported by others. Several types of atypical endometrial hyperplasia which might easily be mistaken for carcinoma have been described recently by Novak and Rutledge.[11]

Fifty cases of combined tumors were found. These cases are summarized in Table I.

Comment on Cases in the Literature

Several observations can be made from this summary. The ovarian tumors were divided into 28 thecomas and 22 granulosa-cell tumors. The greater frequency of thecomas, as compared with granulosa-cell tumors, in association with endometrial adenocarcinoma is all the more striking in that the granulosal tumors are in general far more frequent than those of thecal character. In the first 500 cases of the Ovarian Tumor Registry, for example, only 6 thecomas were encountered, as compared to 67 granulosa-cell carcinomas. This would at once suggest that the granulosal tumors possess a lower degree of carcinogenic capacity, presumably the result of a lower degree of estrogen production. This, as a matter of fact, would be in accord with the views of certain investigators[8, 20] and with the very recent studies of the Biskinds.[17] The latter hold that thecal and not granulosal cells are the source of estrogen, and that the estrogenic effects of granulosa-cell tumors are due to the fact that they also contain varying admixtures of thecal elements. This point will be further touched upon later in this paper.

Fifty-four endometrial and 2 cervical carcinomas were reported. In one case, endometrial carcinoma was combined with sarcoma of the stroma, in another with a leiomyosarcoma of the myometrium and a Grade III epithelioma of the skin, producing what the authors who reported this case considered to be 4 separate neoplastic types in one patient.[6] In addition to having an estrogen-producing tumor, this patient had had the added carcinogenic influence of the actinic rays of x-ray therapy. In spite of the dictum that a tumor "is or is not carcinoma," two cases were accepted by us as "probable adenocarcinoma." These 2 reports, published over 10 years ago, contained too many of the criteria of carcinoma to warrant their exclusion, but were still not complete enough to carry absolute conviction.

Myomas of the uterus were found frequently with the feminizing tumors alone and also with the combined tumors. Of the 135 feminizing tumors reviewed in this survey, in which the uterus was described, 45 per cent were associated with myomas. Two instances of squamous metaplasia of the cervix and one of adenomyosis were described. Only a few reports mentioned the cervix. The importance of the study of the cervix in these cases will be discussed below.

The histories of 26 patients were available for study. A detailed analysis of these histories was made, but will not be presented here. The important findings are summarized in the following paragraphs.

The age distribution of the 26 patients was the same as that seen in patients with endometrial carcinoma unaccompanied by estrogen-producing tumors. The age distribution of 26 patients at the time of diagnosis was as follows:

45 to 50 years	2
50 to 60 years	12
60 to 70 years	8
70 to 80 years	4

TABLE I.

AUTHOR	YEAR	OVARIAN NEOPLASM	UTERINE NEOPLASM	NO. OF CASES	SOURCE	ASSOCIATED CONDITIONS
Schroeder[2]	1922	Granulosa	Probable adenocarcinoma	1	Report of 1 case	None
Szathmary[12]	1923	Granulosa	Adenocarcinoma	1	Report of 9 granulosa-cell tumors	4 patients had myomas
Russell[13]	1940	Granulosa	Probable adenocarcinoma	1	Report of 1 case	Tuberculosis of right tube
Wolfe and Neigus[14]	1941	Thecoma	Adenocarcinoma	1	Report of 8 thecomas	4 patients had myomas
Porter and Bramhall[15]	1941	Thecoma	Adenocarcinoma	1	Report of 1 case	None
Henderson[7]	1942	Granulosa Thecoma	Adenocarcinoma Adenocarcinoma	2 3	Report of 21 granulosa-cell tumors and 9 thecomas	10 patients had myomas
Stohr[1]	1942	Granulosa Granulosa	Adenoma malignum Adenocarcinoma	2* 1	Report of 3 cases	2 patients had myomas 2 patients had squamous metaplasia of cervix
Kirshbaum[16]	1943	Thecoma	Adenocarcinoma	1	Report of 1 case	None
Ingraham, Black, and Rutledge[9]	1944	Granulosa	Adenocarcinoma	3	Report of 3 cases	None
Banner and Dockerty[4]	1945	Thecoma Thecoma Thecoma	Adenocarcinoma Adenocarcinoma of the cervix Epithelioma of the cervix	3 1 1	Report of 23 cases	6 patients had myomas
Hodgson, Dockerty, and Mussey[5]	1945	Granulosa Granulosa	Adenocarcinoma Adenoacanthoma	7† 1	Report of 62 granulosa-cell tumors‡	32 patients had myomas
Woll, Hertig et al.[8]	1948	Thecoma Granulosa	Adenocarcinoma Adenocarcinoma	17 1	Report of 330 cases of adenocarcinoma of the endometrium	Not described
Mussey, Dockerty, and Masson[6]	1948	Granulosa	Adenocarcinoma of endometrium, leiomyosarcoma in myoma, epithelioma of abdominal wall	1§	Report of 2 cases	Myoma
		Granulosa	Adenocarcinoma of endometrium, sarcoma, stroma	1‖		Adenomyosis

*The photomicrographs of these two endometria were interpreted by us as representing endometrial hyperplasia. They are included here because of their acceptance as carcinoma by several others. They are not included in the analysis of 26 cases presented below.
†One patient received 1200 mgm. hours of intracavitary radium three years before granulosa cell tumor was diagnosed.
‡Three of these cases were combined granulosa cell tumors and carcinoma of the breast.
§Received 15 x-ray treatments 21 years before granulosa cell tumor was diagnosed and also intracavitary radium 6 years before diagnosis. All radiation was given because of myoma uteri.
‖Had radium sterilization 6 years before granulosa cell tumor was diagnosed.

In the combined tumors, adenocarcinoma occurs much more frequently[6] but it does not seem to appear at an earlier age. As a matter of fact, almost all of the patients with the combined group were postmenopausal, and the possible significance of this observation will be discussed later in this paper.

As expected, the presenting symptom was postmenopausal bleeding, this being noted in 85 per cent of the patients. This bleeding was of much longer duration than is seen with endometrial carcinoma alone. Seventy per cent of the 20 patients in whom the bleeding was described had bled intermittently for 2 to 10 years. For reasons discussed later, it seems logical to suspect that many of these patients had bled from a hyperplasia for years before the appearance of carcinoma.

Treatment of 22 patients was described. Twenty-one were treated by total hysterectomy and bilateral salpingo-oophorectomy. One patient was treated by subtotal hysterectomy and removal of the adnexa. Four patients were given preoperative radiation. The value of radiation of feminizing tumors has not been clearly established.

A follow-up was available on only 16 patients, and this small group can scarcely be of much statistical value. One patient died of operative shock. Four died of carcinoma within two years. Eight were well one to five years after operation. Three patients were well five or more years after operation. This falls within the expected salvage rate of patients with 2 neoplasms, one malignant and the other sometimes malignant. Many granulosa-cell tumors which appear benign are capable of late recurrence. The curability of granulosa-cell tumors is not as great as was formerly believed. Jones and Te Linde[18] have reported recurrences in 3 patients fifteen to twenty-one years after operation. Studies of the large group of feminizing tumors in the Ovarian Tumor Registry, already under way, should throw light on the degree of malignancy of this tumor group.

Method of Study of New Cases

Sixty-six consecutive cases of feminizing tumors of the ovary encountered in the Laboratory of Gynecological Pathology of the Johns Hopkins Hospital were reviewed. These cases will not be reported in detail in this paper, but a few points concerning them are pertinent to this discussion.

Thirty-three patients were of postmenopausal age, 30 were of menstrual age, and 3 were children of pubertal age.

In 29 cases the endometrium was available for study. Sixteen endometria showed definite hyperplasia, 7 were of proliferative or atrophic type, and one was in the secretory phase.

Five patients had received radiation because of abnormal bleeding a number of years before a diagnosis of granulosa-cell tumor was made. Four patients had received deep x-ray therapy 2 to 20 years prior to diagnosis. One patient received intracavitary radium 5 years prior to diagnosis.

Four instances of combined feminizing mesenchymomas of the ovary and adenocarcinomas of the endometrium were found. All 4 of these occurred in postmenopausal women, representing 12 per cent of the postmenopausal group. Two of these were sent in from outside clinics and laboratories. We are grateful for permission to include them in the present study and proper acknowledgment is made in the case reports appended below. An additional case of combined feminizing mesenchymoma of the ovary and carcinoma of the breast is included in this report.

CASE 1.—This 60-year-old white married woman, para vi, presented herself because of vaginal spotting of 3 months' duration. An uneventful menopause had occurred at age 50. The right ovary had been removed for unknown reasons before the menopause.

On pelvic examination the uterus was thought to be enlarged to 4 times normal size and to be myomatous and fairly mobile. No ovarian tumors were identified. Myoma or sarcoma of the uterus was suspected. Panhysterectomy and removal of the remaining adnexa were done. (E. N.) The uterus measured 10 by 7 by 3 cm. The cavity was filled with what grossly appeared to be adenocarcinoma. The left ovary was replaced by a solid tumor mass measuring 10 by 13 by 7 cm. On its smooth surface were a few papillomas. On cut section the tumor was firm, homogeneous, and dull tan in color.
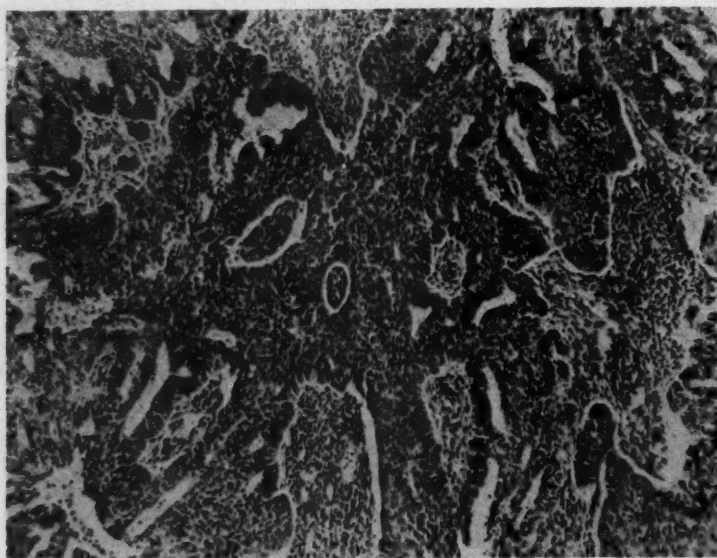
Fig. 1.—Adenoacanthoma of endometrium in Case 1.
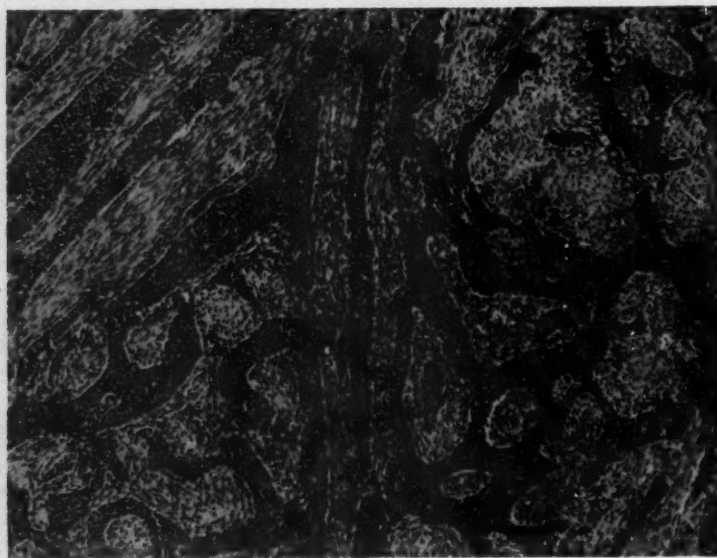
Fig. 2.—Granulosa-cell carcinoma of cylindromatous pattern in Case 1. Note the dark-staining anastomosing cylinders of granulosal cells separated by the light-staining trabeculae of connective tissue.

Microscopic Examination.—The cervix was normal. The endocervix showed marked squamous metaplasia. Sections through the fundus showed a definite adenoacanthoma with extensive invasion of the myometrium. The glands were replaced by carcinomatous tissue

which showed many mitotic figures, hyperchromatosis, variation in cell size and squamous metaplasia (Fig. 1). Sections of the ovary showed typical granulosa-cell carcinoma. There were many mitotic figures. In some areas the carcinoma was solid. In others long discrete cylindromas were separated by trabeculae of hyaline and fibrous tissue (Fig. 2). These trabeculae contained many whorl-like strands of plump fusiform theca cells. In a few fields the folliculoid pattern of granulosa cells is predominant (Fig. 3).

The patient is well 4 years after operation.

Final Diagnosis.—Granulosa-cell carcinoma of the left ovary, adenoacanthoma of the endometrium, squamous-cell metaplasia of the cervix.
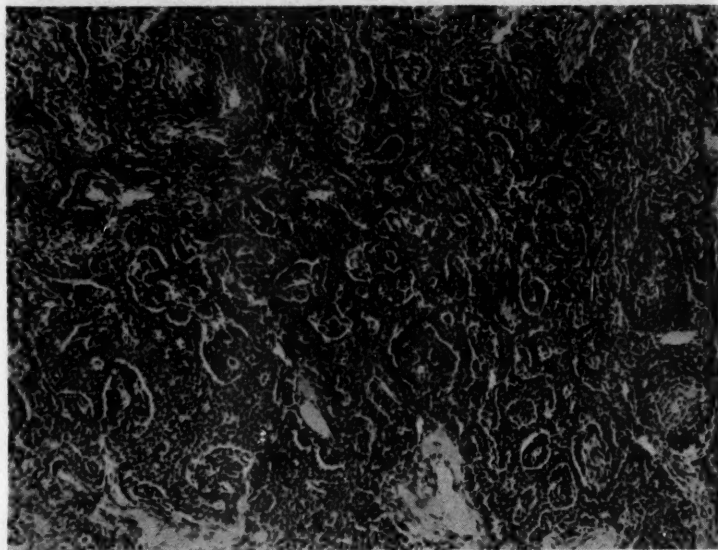
Fig. 3.—Another area, of follicular pattern, in granulosa-cell carcinoma of Case 1.

CASE 2 (Courtesy of Dr. G. W. Mylks, Jr., and Dr. John Hamilton, Kingston, Ontario).— This 54-year-old white married woman, para ii, consulted her physician because of vaginal spotting of one week's duration. Her menses had ended with a normal menopause at the age of 49.

Pelvic examination revealed a firm, mobile mass in the right adnexa rising to the level of the umbilicus. The uterus was slightly enlarged.

A total hysterectomy and bilateral salpingo-oophorectomy were done. A yellow, lobulated, firm, pedunculated tumor 12 cm. in diameter replaced the right ovary. On cut section it showed several small cystic areas and a few areas of hemorrhage. Many yellow lobules of tissue were separated by fibrous trabeculae. The endometrial cavity contained a typical adenocarcinoma high in the fundus. There was gross invasion of the myometrium. The left ovary was atrophic.

Microscopic Examination.—The ovarian tumor was made up almost entirely of granulosa cells in large clumps separated by fibrous trabeculae. In a few fields, large, whorl-like strands of typical theca cells were present. Both the diffuse folliculoid and the pseudo-adenomatous pattern of granulosa cells were seen. Sections of the uterus showed adenocarcinoma of the endometrium, Grade II, invading the myometrium (Fig. 4). No sections of the cervix were available.

The patient is well 18 months after operation.

Final Diagnosis.—Granulosa-theca-cell tumor of the right ovary, adenocarcinoma of the endometrium.

CASE 3 (Courtesy of Dr. Ernest E. Aegerter, Philadelphia, Pa.).—This 64-year-old white woman was first seen because of postmenopausal bleeding. Curettement and microscopic examination of the tissue established a clear-cut diagnosis of adenocarcinoma of the endometrium. The patient received 3 implantations of intracavitary radium. Four years later she developed ascites, constipation, and difficulty in initiating urination. Neoplastic invasion of the bladder was seen on cystoscopy.
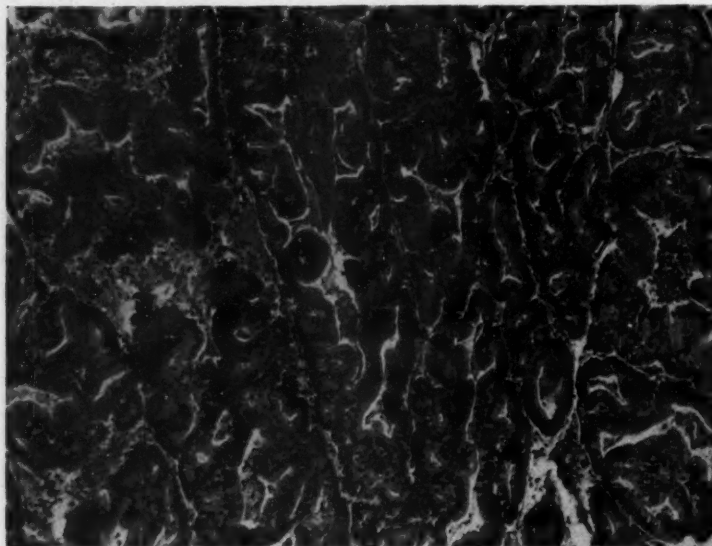
Fig. 4.—Endometrial adenocarcinoma of Case 2.
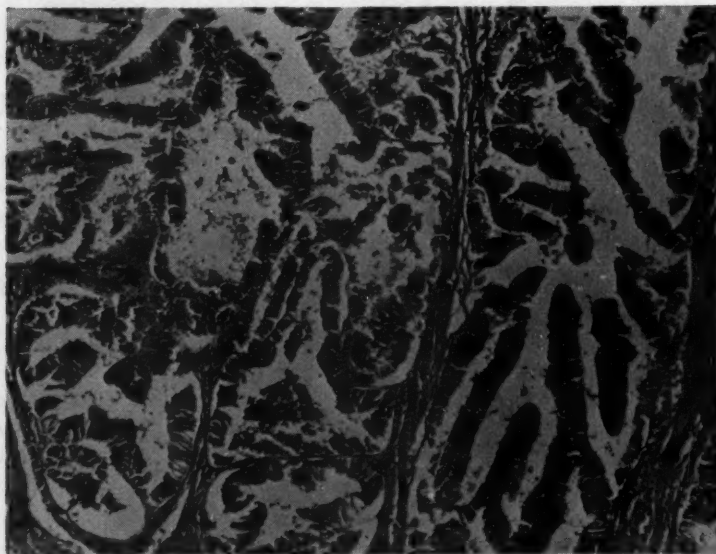
Fig. 5.—Endometrial carcinoma of Case 3.

Laparotomy showed the peritoneum to be studded with tumor tissue which arose from a large carcinoma of the right ovary. A biopsy of the tumor mass was interpreted by the hospital pathologist as ''theca-cell tumor,'' and by us as ''granulosa-cell carcinoma.'' The patient was given x-ray therapy but she went rapidly downhill and died 2 months later.

Autopsy showed most of the abdominal viscera invaded by the tumor. The ovarian carcinoma had almost entirely replaced the uterus. Pulmonary metastases were found.

Microscopic Examination.—Biopsy of the ovary showed a typical granulosa-cell carcinoma. The morphology of the cells as well as their tendency to arrange themselves in clusters and rosettes were characteristic. There were many mitoses and much hyperchromatosis indicating a considerable degree of malignancy. The uterine curettings showed definite endometrial adenocarcinoma (Fig. 5).

Final Diagnosis.—Granulosa-cell carcinoma, adenocarcinoma of the endometrium.
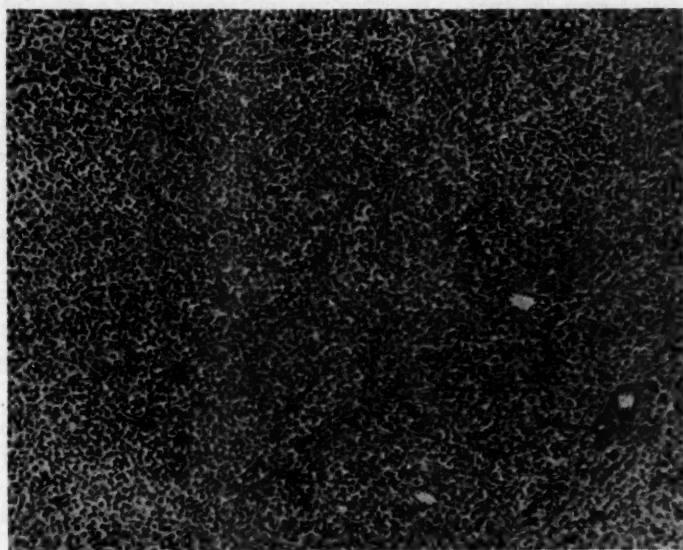
Fig. 6.—Thecoma with strong granulosal admixture in Case 4.
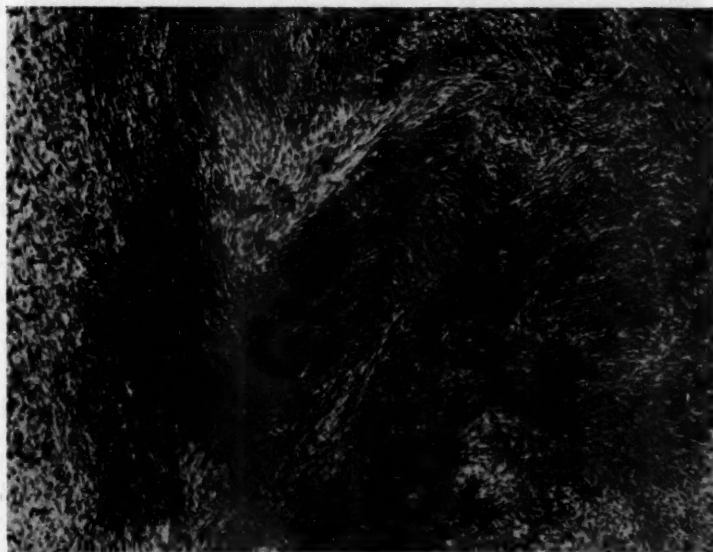
Fig. 7.—Fat stain of thecoma in Case 4.

CASE 4.—This 73-year-old white single woman, para 0, first sought aid after 12 years of postmenopausal vaginal spotting. Her menses had been normal and had ended with uneventful menopause at age 50. Pelvic examination had been refused on many occasions in the past 10 years. She had had severe hypertension for many years. A recent cerebral thrombosis had produced a partial paraplegia.

On pelvic examination the cervix was normal. The uterus was found to be immobilized by a mass of neoplastic tissue which extended to the right pelvic wall. A mobile mass 20 cm. in diameter was palpated in the left adnexa. Curettement yielded a large quantity of tissue which showed "adenocarcinoma, Grade IV." She was given 3,506 mg. hr. of intracavitary radium. (Dr. J. Donald Woodruff.)

Eight days later laparotomy was done. Carcinoma was seen to penetrate the right uterine wall and to extend into the right great vessels and pelvic wall. The right adnexa, bladder, and sigmoid were involved. The left ovary was replaced by a solid, discrete, smooth, pale-yellow tumor 12 cm. in diameter. The left tube was enlarged to 4 by 4 by 10 cm. by a simple hydrosalpinx. A total hysterectomy, bilateral salpingo-oophorectomy and removal of as much tumor as possible were done.

Microscopic Examination.—Sections of the left ovarian tumor showed plump, fusiform cells arranged in whorls characteristic of the thecoma. Fat stains showed fat within the cells (Fig. 6). Sections of the uterus show a Grade IV adenocarcinoma invading the myometrium in broad sheets and in pegs of tissue (Fig. 7). Glandular elements were present in about 1 out of 4 fields. The endocervix showed marked squamous-cell metaplasia.

The patient is well 6 months after operation.

Final Diagnosis.—Thecoma of the left ovary, adenocarcinoma of the endometrium, Grade IV, squamous metaplasia of the cervix.

The report of an additional case, representing a combination of granulosa-cell carcinoma and carcinoma of the breast is also appended.

CASE 5 (Courtesy of Dr. O. Benwood Hunter, Jr., Washington, D. C.).—This 42-year-old white woman was referred to her gynecologist because of prolonged and profuse menses of 5 months' duration. She had had no previous menstrual irregularities. A radical mastectomy had been done because of adenocarcinoma of the left breast one year before the onset of the menorrhagia.
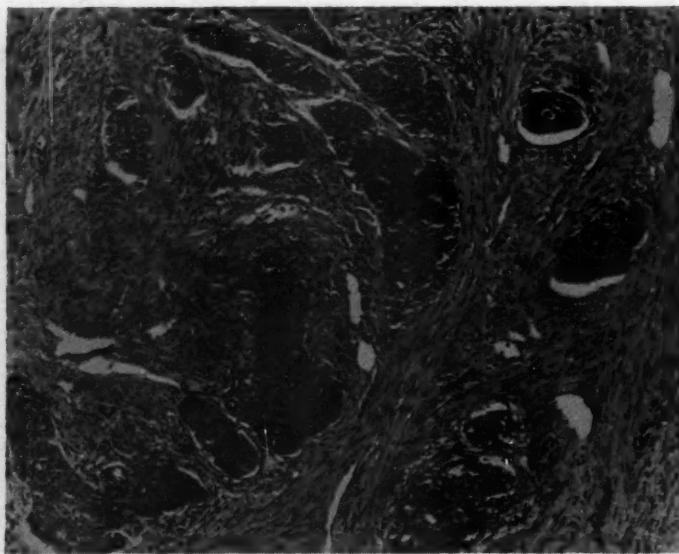
Fig. 8.—Myometrium of Case 4, showing invasion of very anaplastic endometrial adenocarcinoma, which here resembles epidermoid type, though original curettings definitely showed gland pattern.

Pelvic examination showed a cyst 12 cm. in diameter on the left ovary and another cyst 10 cm. in diameter on the right ovary. The uterus appeared normal. A bilateral oophorectomy was done. Seven months later the patient underwent a radical mastectomy for adenocarcinoma of the right breast.

Microscopic Examination.—A section of the solid tissue at the margin of the left ovarian cyst was sent for study. It showed a very diffuse and uniform distribution of granulosa cells. A few Call-Exner bodies were seen. There were a few mitotic figures but no hyperchromatosis or rosettes were seen (Fig. 8). No slides of the breast carcinoma are available.

The patient is well 1 year after the second mastectomy.

Final Diagnosis.—Granulosa-cell tumor of the left ovary, adenocarcinoma of both breasts.

Comment

The collection of a total of 54 cases of combined feminizing mesenchymomas of the ovary and uterine carcinoma demonstrates that this combination is by no means rare. Dockerty found that 27 per cent of postmenopausal women with feminizing tumors also had endometrial carcinoma,[6] and he estimates its incidence to be 100 times greater in the presence of feminizing tumors. Hertig[19] estimates that 18 to 20 per cent of granulosa cell tumors are accompanied by uterine carcinoma. In our group of 33 postmenopausal women with feminizing tumors, 12 per cent had carcinoma of the endometrium. In the total of 54 cases, fully 29 were thecomas, in spite of the much lower incidence of thecomas in general as compared with granulosa-cell tumors. Both types of tumors are undoubtedly estrogenic, but the question has been raised as to whether the activity of the granulosal group in this respect is due to the admixture of thecal elements.[20] Further study will be necessary before this concept can be accepted.

Studies of estrogen-producing tumors by the use of ketosteroid-specific stains are now in progress by several groups.[20, 21] It is hoped that the specific stains will give a more accurate indication of the estrogen production of various tumors. The histologic classification of the feminizing tumors in use at present is at best a crude index of their functional capacity.

In the group of patients presented, uterine carcinoma occurs much more frequently in the presence of feminizing tumors, but it does not seem to occur at an earlier age. This group is too small to be conclusive, but the findings do seem to bear out Loeb's theory that the tissues must remain under the influence of estrogens for a prolonged period of time before estrogens can exert a carcinogenic effect.[23]

This theory would also explain why so few endometrial carcinomas have been attributed to estrogen therapy.[24, 25] This therapy is rarely given over a period of time long enough to allow the estrogens to become carcinogenic. Because of the strong refractoriness of lower animals to the development of endometrial carcinoma, this neoplasm has never been produced experimentally by the administration of estrogens.

Several years ago, Novak and Yui[26] observed that endometrial hyperplasia frequently co-exists in the same uterus with endometrial adenocarcinoma. Because of this and because of the occasional marked histologic similarity between the two lesions, they predicated that, in certain genetically predisposed postmenopausal women, endometrial hyperplasia was capable of transformation into endometrial carcinoma. Several observations in this group of patients support this concept. Seventy per cent of the 20 patients in whom postmenopausal bleeding was described had bled intermittently for 2 to 10 years. It is unlikely that these patients could have survived this long in the presence of carcinoma. Some source of bleeding other than carcinoma and existing prior to the appearance of carcinoma must be presumed. Endometrial hyperplasia is known to accompany a majority of estrogen-producing tumors. One may at least suspect that many of these patients bleed for years from a hyperplasia and that this hyperplasia finally gives rise to carcinoma.

In the presence of estrogen-producing tumors in postmenopausal women, endometrial carcinoma occurs quite frequently, while combined carcinoma of the cervix and breast occurs rarely. Again this series is too small to be conclusive, but it suggests that the degree of carcinogenic response of each of these tissues to estrogens in postmenopausal life parallels their degree of physiologic response to estrogens during menstrual life.

The frequent occurrence of myomas of the uterus with estrogen-producing tumors is of interest, but it is doubtful that this can be interpreted as evidence that myomas represent a response to hyperestrogenism, as has been suggested by Meigs.[27]

Squamous metaplasia of the cervix was found in 2 of the 5 cases of combined tumors reported by us. Stohr[1] found this lesion in 2 of the 3 cases of combined tumors reported by her and considered it to be a response to hyperestrogenism. Overholser and Allen[28] produced squamous metaplasia of the cervix in monkeys by trauma and estrogen administration. In women, squamous metaplasia of the cervix has never been proved to be a response to hyperestrogenism, although this view has been suggested. Careful study of the cervix in a large group of cases of combined tumors may help to clarify this problem.

It was noted that 5 of the 66 patients with feminizing mesenchymomas had had previous pelvic radiation. The work of Furth and Butterworth[29] in the production of granulosa-cell tumor in mice by x-ray radiation is well known. Traut and Butterworth[30] have mentioned one patient and McKay and his co-workers[29] have reported one patient in whom thecomas occurred following pelvic radiation. It can certainly not be assumed that radiation caused the development of feminizing tumors in these 5 patients, but the possibility offers interesting speculation.

Although they do not bear directly on the subject, two recent contributions on the etiology of feminizing tumors should be mentioned. Woll and his co-workers[8] have approached the subject of the combined tumors from a viewpoint different from that of most investigators. They suggest that feminizing tumors of the ovary may be secondary to the endometrial carcinoma. They theorize that the absorption of the products of protein catabolism from the necrotic carcinoma stimulates the secretion of pituitary luteinizing hormone. This LH, acting with the existing FSH, might conceivably stimulate the ovarian cells capable of response, thus causing the growth of thecomas or granulosa-cell tumors. They further suggest that the protein catabolism caused by x-ray might set off this chain of events, thereby giving rise to feminizing tumors. The evidence for this startling new concept is still lacking.

Several interesting experiments in ovarian transplantation have recently been reported. Biskind and Biskind[31] and others have castrated mice and implanted one of the ovaries in the spleen. The estrogens from the ovary are thus carried through the portal circulation into the liver, where they are inactivated. The resulting fall in estrogens and the compensatory rise in pituitary gonadotropins is believed to stimulate the growth of luteomas and granulosa-cell tumors in the transplanted ovary. This experiment has been confirmed by Li and Gardner[32] by transplantation of the ovary to the pancreas in mice.

The endometrial carcinomas in the combined tumors might at first appear to represent a small minority of the carcinomas which develop under stimulation of overwhelming amounts of estrogen. The majority of endometrial carcinomas occur after the menopause and would seem to have no relation to hyperestrogenism. Yet there is evidence of hyperestrogenism during and after the menopause in many patients with endometrial carcinoma. This disease is rare in oophorectomized women, although cases have been reported.[33, 34] Late menopause and absence of menopausal symptoms are frequently found in patients

with endometrial carcinoma.[35, 36] Increased estrogenic activity has been found in the vaginal smear of a majority of these patients.[37] Endometrial hyperplasia was found accompanying endometrial carcinoma in 25 per cent of the patients studied by Novak and Yui.[26] In a study of 331 endometrial carcinomas, Woll and his co-workers[8] found that ovarian thecomatosis was 4 times more frequent and thecomas 9 times more frequent in the carcinoma patients than in the controls.

These observations indicate that hyperestrogenism of varying degree frequently accompanies endometrial carcinoma. Hyperestrogenism appears often to be the added factor which initiates carcinogenesis in women already predisposed to cancer. The cases of combined tumors represent the most extreme examples of this process, and therefore offer one of the best opportunities for its study.

Very few endocrinological studies have been done on patients with the combined tumors because they are seldom recognized before operation. A few studies, however, have been made by several investigators, using various methods of assay. The results are therefore not comparable or conclusive. Clinical awareness of the condition should lead to a more frequent preoperative diagnosis. A simple, accurate method of blood or urine estrogen assay, now sought by several groups, would be a great aid in screening suspected patients and in studying patients with combined tumors. Investigation of the combined tumors by hormone assays and specific stains should yield valuable information on the etiology of endometrial carcinoma.

Summary

Fifty cases of combined feminizing mesenchymomas of the ovary and carcinoma of the uterus were collected from the literature. The histories of 26 of these patients were critically examined.

In a study of 66 feminizing mesenchymomas of the ovary in this laboratory, 4 cases of combined feminizing mesenchymomas and endometrial carcinoma were found. These 4 cases comprised 12 per cent of the postmenopausal group with feminizing tumors. The report of these cases brings the total number of recorded cases of combined tumors to 54. One case of combined granulosa-cell tumor and adenocarcinoma of the breast is also reported.

Feminizing tumors of the ovary in combination with uterine carcinoma occur more frequently than is commonly realized. Various investigators have found that 15 to 27 per cent of postmenopausal women with feminizing tumors develop endometrial carcinoma.

In the 54 cases of combined tumors, the thecoma occurred more often in combination with uterine carcinoma than did the granulosa-cell tumor, in spite of the much greater general incidence of the granulosal tumor. This suggests that the thecoma, by means of greater estrogen production, has the greater carcinogenic effect. It supports the concept that the thecal and not the granulosal cells are the sole or chief source of estrogen. The greatest carcinogenic response to tumor-produced estrogens occurs in the endometrium. Cervical and mammary carcinomas are seen only occasionally in combination with estrogen-producing tumors. The degree of carcinogenic response of these tissues to estrogens in postmenopausal life seems to parallel the degree of physiological response during menstrual life.

A study of 26 case histories, still too few to be conclusive, indicates that, although feminizing tumors cause a greatly increased incidence of endometrial carcinoma, they do not seem to incite the appearance of this lesion at an age earlier than is noted in patients with endometrial carcinoma alone. Prolonged estrogen stimulation, rather than temporary intense estrogen stimulation, appears to be necessary for carcinogenesis.

Several observations in these 26 cases support the concept that endometrial hyperplasia, in some predisposed postmenopausal women, occasionally is capable of transformation into carcinoma.

Evidence is presented that, in the majority of cases of endometrial carcinoma, hyperestrogenism of varying degree is present. This hyperestrogenism seems to be the one added factor that sets off carcinogenesis in a postmenopausal woman already genetically predisposed to cancer. The cases of combined tumors are thought to represent the most extreme examples of this process. Therefore they offer an excellent opportunity for the study of the etiological role of estrogens in carcinoma of the endometrium.

Clinical awareness, early preoperative diagnosis, and thorough endocrinological investigation of the combined tumors should throw additional light on this problem in coming years.

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26 EAST PRESTON STREET

Discussion

DR. VIRGIL S. COUNSELLER, Rochester, Minn.—It is most significant that the greatest carcinogenic response to tumor-produced estrogens occurs in the endometrium, and that cervical and mammary carcinomas are only occasionally seen in combination with estrogen-producing tumors; the effect of the estrogens on these tissues in postmenopausal life does seem to parallel the degree of physiologic response during menstrual life as suggested.

My colleagues at the Mayo Clinic and I are in complete agreement in most respects with the thesis and conclusions as presented. It is not possible to deal at this time with all of the interesting data but I should like to stress a few points briefly which have occurred to us. It is of interest that other evidence indicates that estrogen does play an important role in the development of uterine carcinoma. For example, uterine carcinoma is rarely seen in patients whose ovaries have been surgically removed, even though the adrenal glands continue to supply estrogen in small amounts. Ayre and Bault have observed that vaginal smears of a group of women with malignant uterine lesions showed evidence of sustained estrogenic activity. Also, Randall and others have noted that patients with fundal carcinomas have a late menopause and have unusually mild symptoms thereof. The case reported by Fremont-Smith and his associates further emphasizes the carcinogenic effect of estrogens. Their patient, aged 43 years, had accidentally received almost 12,000,-000 rat units of estrogen over a period of eight years because of severe menopausal symptoms. Serial samples of endometrium removed by curettage during the eight years showed the development from endometrial hyperplasia to carcinoma. Green observed a high incidence of fundal cancers in old rabbits which had had repeated attacks of toxemia of pregnancy so that the destruction of circulating estrogens by the liver ceased to occur. The observation of Speert, that patients with cirrhosis of the liver showed a high incidence of fundal carcinoma, would support Green's contention. The damaged liver permitted a high concentration of hormone in the circulation which exerted a carcinogenic effect among certain patients who were susceptible to the development of cancer.

Significant, also, is the fact that uterine or fundal cancer is rarely seen in persons less than 40 years of age, and when it does occur the patients have a very irregular irregularity of their menses. There is little evidence of ovulation. We know, too, that functioning tumors of the ovary suppress ovulation.

Drs. Dockerty and M. Elizabeth Mussey, who recently studied 87 mesenchymomas encountered at the Mayo Clinic, found also associated endometrial carcinomas in 15 instances; in 3 of these 15 instances there were, in addition, cancers of the breast, 1 of which occurred bilaterally. They also noted that uterine cancer did not complicate mesenchymomas of younger women. Our department has discussed this point on several occasions, and we think it is very significant from the therapeutic and also the carcinogenic standpoint. Loeb's theory appears to be a satisfactory answer to date; namely, that the tissues must remain under the influence of estrogens for prolonged or sustained periods of time before they are able to exert a carcinogenic effect. I should like to add that there surely must be a biologic susceptibility to cancer of varying degree in different family strains which might be a statistical factor to contend with eventually. From a therapeutic standpoint it becomes rather alarming when we discover that today 1 of 5 women under the age of 40 is receiving estrogens. With the average dose they may not be harmful, especially if all of the other organs are functioning normally, but the case of Fremont-Smith in which uterine cancer did develop after sustained continuous dosage of estrogens should at least be a warning against using excessive estrogenic substances for long periods.

It seems doubtful to us that radiation effect has anything to do with the development of mesenchymomas although the possible significance of the production of granulosa-cell tumors in mice by roentgen radiation by Furth and Butterworth cannot be ignored. Intrauterine radiation and roentgen therapy have been given in small doses for menopausal menorrhagia to a tremendous number of patients in the past and at present, yet the number of these tumors is not large.

The difficulty sometimes encountered in recognizing or distinguishing between carcinoma and atypical hyperplasia is great, especially since so many women nowadays are receiving estrogenic therapy. Occasionally, the department of pathology will ask, after looking at the frozen sections, if the patient has been on estrogen therapy since there are all stages of activity noted in the particular slide. I can readily understand the mistakes which might arise in therapy unless one has access to a competent and experienced pathologist.

We certainly owe much to Dr. Novak and his co-workers for calling to our attention as early as 1936 the fact that endometrial hyperplasia frequently coexists in the same uterus with endometrial adenocarcinoma, and that there is considerable evidence of hyperestrogenism in these postmenopausal patients such as lateness of the menopause and its freedom from distressing symptoms, and increased estrogenic activity as indicated by vaginal smears. One cannot say that all patients with endometrial hyperplasia are candidates for uterine carcinoma, but when in at least one-fourth of the cases such hyperplasia is associated with carcinoma one strongly suspects that there is a very close relationship. Therefore, since hyperplasia is related to estrogenic influence and this in turn to carcinoma, it becomes quite understandable and significant that mesenchymomas are found associated with uterine cancer much more frequently than could be explained on the basis of chance alone.

DR. HERBERT E. SCHMITZ, Chicago, Ill.—In reviewing a paper by Dr. Malcolm Dockerty relative to the occurrence of carcinoma of the endometrium in women under 35 years of age, I came across his observation that in all of these patients there had been a previous bleeding problem and a high incidence of hyperplasia of the endometrium. I, therefore, reviewed our own incidence and found that we had nine endometrial carcinomas in women under 35 years of age, and in each instance there had been this bleeding problem with a record of numerous curettages before the carcinoma had developed. I think it is a very important observation, and it should be brought to our attention in the management of bleeding problems, that signs of hyperestrinism in young women are associated with a higher incidence of carcinoma of the endometrium.

DR. C. L. RANDALL, Rochester, Minn.—There have been numerous contributions by the Fellows of this Association concerning estrogen effect and the ultimate development of adenocarcinoma of the uterus. Broders and associates studied early carcinomas of the uterus and reported the uninvolved portions of the endometrium to be atrophic rather than hypertrophic. There have been other reports discrediting the apparently significant observation that adenocarcinoma of the uterus does not develop after bilateral oophorectomy. One point I have so far not heard adequately discussed is that of the possibility of adenocarcinoma developing in the presence of an atrophic vaginal smear. There certainly are a number of institutions doing routine cytology, but I have never heard of, nor seen reported, a single case of endometrial carcinoma discovered in a woman showing an atrophic smear. Several years ago we called attention to the fact that we had never observed an atrophic vaginitis associated with adenocarcinoma of the uterus. Surely smears and cytology should be yielding some additional and convincing evidence on this point.

DR. NOVAK (Closing).—Dr. Counseller has very correctly emphasized that duration and persistence of estrogen dosage rather than intermittent even though very large dosage are likely to predispose to the development of cancer. He also spoke of the infrequency of endometrial hyperplasia after bilateral oophorectomy, but a recent case of my own illustrates that it can occur, presumably as a result of extraovarian, probably adrenal, estrogen production. This patient had had the adnexa of both sides, but not the uterus, removed in

her early forties, with resulting menopause. More than 10 years later she developed uterine bleeding, with a moderate diffuse enlargement of the uterus. The endometrium of the removed uterus showed atypical diffuse Swiss-cheese hyperplasia, and a careful search of the pelvis revealed no residual or aberrant ovarian tissue.

So far as I know, the hyperplasia which is so common in women during reproductive life has no tendency toward cancer development. On the other hand, I believe that postmenopausal exposure of the endometrium to persistent estrogen stimulation may not only produce hyperplasia, though not always of diffuse extent, but that it does predispose to the development of carcinoma, probably, on the basis of animal experiments, in those women who are already genetically predisposed to cancer. Whether rightly or wrongly, I have been teaching students what I believe is a crystallization of the far-flung cancer studies being made in many fields of science. These indicate that the cancer cell is a normal body cell which, for some as yet unknown reason, undergoes transformation into the killer cell of cancer. Whether this change be a somatic mutation, as many call it, no one knows, but the evidence indicates that heredity plays at least some part in this unknown cell surge, and that the intrinsic cell change may be influenced by such extrinsic factors as chronic irritation, whether this be of mechanical, inflammatory, chemical, or endocrine nature. The role of viruses and the so-called milk-borne factor is not as yet understood. There are some women in whom the cancer genetic tendency is so strong that they will inevitably develop a cancer somewhere and sometime, without any contributing chronic irritation. We thus often find early cancer in clean or innocent-looking cervices. In others a combination of intrinsic and extrinsic factors is required for the development of cancer. Finally, there are patients lucky enough to have little or no genetic tendency to the disease, so that we see women who have had ugly, infected, and eroded cervices for many years, without the development of cancer.

A CLINICAL STUDY OF GRANULOMA INGUINALE WITH A ROUTINE FOR THE DIAGNOSIS OF LESIONS OF THE VULVA*

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GRANULOMA inguinale is a specific, chronic, supposedly infectious, granulomatous disease, caused by a gram-negative bacillus, *Donovania granulomatis,* Anderson,[1] 1943, or the so-called "Donovan body" first described by Donovan[2] in 1905. Extragenital and generalized infections have been described but lesions occur most commonly in the genital and the perigenital regions. The disease is regarded as one of the venereal diseases but its mode of transmission is not definitely known. Absence of lesions in known contacts is the rule rather than the exception.

Granuloma inguinale was described clinically by several investigators prior to Donovan's description of the etiological agent. Most of the important facts, however, have been discovered during the past ten years.

The infection is seen in the United States almost exclusively in the Negro race and probably for this reason is more prevalent in the Southern states. There appears to be little if any evidence of racial immunity. Granuloma inguinale is said to be more common in the male and occurs more frequently in the so-called venerealogic group which shows a high incidence of other venereal diseases.

Etiology

There has been agreement for many years that the finding of Donovan bodies in tissue established the diagnosis of granuloma inguinale. Despite contrary reports in the literature, the nature of these bodies remained in doubt until 1943, when Anderson[1] reported the cultivation of a morphologically similar organism in the yolk sac of the developing chick embryo. Dienst, Greenblatt, and Sanderson[3] and later Carter, Jones, and Thomas[4] had failed to cultivate the bacillus by inoculating the chorioallantoic membrane. Anderson described the organism as a bacillus which required living cells for growth. Because of the nature of the infection and the cultural requirements of the organism, she established a new genus and named the bacillus *Donovania granulomatis.*

Anderson's work has been confirmed and the identity of the bacillus established by a number of different investigators. There seems little doubt at the present time that *Donovania granulomatis* is the organism described by Donovan and that it is the etiological agent of granuloma inguinale.

Diagnosis

The specific diagnosis of granuloma inguinale should always be based upon the demonstration of morphologically typical intracellular bacilli in

tissue smears. The tissue should be taken from the most friable, granulating, and basal portion of the lesion. Although the diagnosis usually depends on the demonstration of typical intramonocytic organisms, experienced workers frequently make the diagnosis by finding the encapsulated bacilli extracellularly. However, unless the examiner has had experience, it is best to repeat the biopsy until typical intracellular bacilli are found. Identification is directly related to the experience of the examiner.

Fig. 1.—Upper, Granuloma inguinale with massive hypertrophy of the vulva. Lower, Primary granuloma inguinale of the anterior cervix.

Smear Preparation.—Biopsy forceps are used in our clinic to obtain the tissue. A site is selected that appears to be the most acute. This is usually not a marginal biopsy but a basal one. Small pieces of tissue are rubbed between

two glass slides to prepare the smears. After drying in the air they are stained immediately with either Wilson's or Wright's stain. The staining technique is identical with that used for staining blood smears with the exception of a slight prolongation of the staining time before dilution with distilled water. Staining times will vary slightly with different stain preparations. In smears prepared and stained in this manner some of the cells may be ruptured and the bacilli seen extracellularly.

Fig. 2.—Upper, Ulcerative granuloma of the vagina and vulva. Lower, Granuloma of the vulva with a pseudo bubo.

An intradermal test and a complement fixation test have been described. Nonspecific and cross reactions occur and neither test is so satisfactory for diagnosis as is the tissue smear.

Differential Diagnosis

Granuloma inguinale must be differentiated from syphilis, carcinoma, lymphopathia venereum, chancroidal infection, tuberculosis, blastomycosis, condyloma acuminatum, or any of the granulomatous diseases.

Clinicians in the South see many patients with hypertrophic, ulcerative, bubo-forming, sinus-forming, and stricture-forming pudendal and perigenital lesions. The bizarre appearance of these diseases is recognized. Combinations of various diseases in the same patient are common. Inspection and palpation rarely give more than a clue to the proper tests to use for diagnosis. Frequently secondary infection changes the appearance of the primary lesion in a way that makes difficult the demonstration of the specific etiological agent. Differential diagnosis can best be accomplished by close cooperation between the clinician, bacteriologist, and pathologist. A definite diagnostic routine[5] has been used in the Gynecologic Clinic at Duke Hospital for the study of these diseases. Table I shows a group of 772 patients who were studied by one or more of the laboratory procedures listed in Table II.
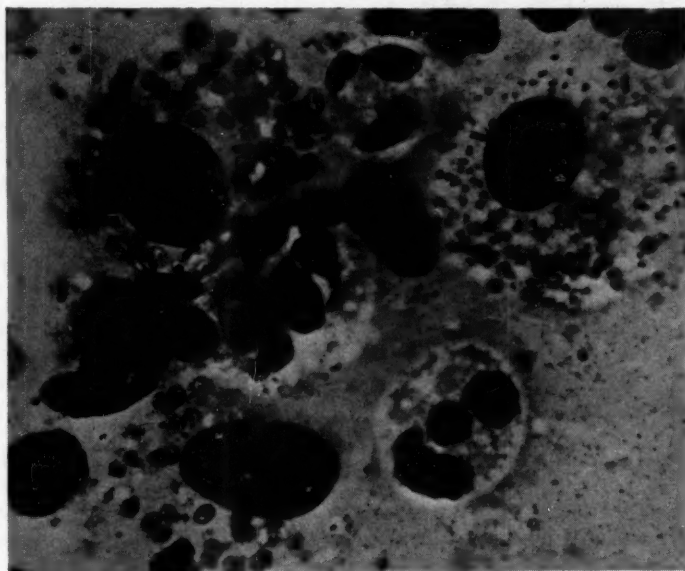
Fig. 3.—Tissue smear preparation stained with Wilson's stain showing three cells with Donovan bodies in various stages of development.

Material

The present report deals with 79 female patients with granuloma inguinale seen in the Duke Gynecology Clinic. A specific diagnosis was made on all of these patients by the tissue smear examination and demonstration of morphologically typical Donovan bodies. Thirty-seven biopsies on these patients were submitted to the pathologist and only 9 were returned with positive diagnoses of granuloma inguinale.

Thirty-two of the 79 patients had syphilis: 18 had secondary fusospirochetosis, 9 had chancroid, 6 had lymphopathia venereum, 3 had condylomata acuminata, and one had carcinoma of the vulva.

The age group was from 16 years to 70 years with an average age of 28.8 years. There were 14 patients under 20 years; 42 in the 21 to 30 year group;

TABLE I. RESULTS OF DIAGNOSTIC STUDIES ON 772 PATIENTS

PRIMARY DIAGNOSIS	NO. PATIENTS	SYPHILIS	ASSOCIATED RELATED DIAGNOSES						
			SENSITIVITY CHANCROIDAL ANTIGEN	LYMPHOPATHIA VENEREUM	GRANULOMA INGUINALE	SECONDARY FUSO-SPIROCHETOSIS	HERPES	CONDYLOMA ACUMINATUM	MALIGNANCY
Syphilis	101	—	10	2	0	22	0	1	0
Lymphopathia venereum	136	54	24	—	0	17	1	0	1
Chancroidal infection	80	4	—	2	0	8	0	3	0
Granuloma inguinale	79	36	9	6	0	18	0	0	1
Herpes	16	0	2	0	0	0	0	0	0
Primary fusospirochetosis	8	0	0	0	0	0	0	0	0
Condyloma acuminatum	63	15	0	0	0	8	0	—	1
Tuberculosis	5	0	0	0	0	0	0	0	0
Pyogenic infections	55	0	0	0	0	0	0	0	0
Malignancy	37	0	0	1	1	5	0	0	—
Mycotic infections	14	0	0	0	0	0	0	0	0
Miscellaneous	137	0	0	0	0	0	0	0	1
Failed to return for completion of studies	40	—	—	—	—	—	—	—	—

11 in the 31 to 40 year group; 7 in the 41 to 50 year group; 3 in the 51 to 60 year group, and two in the 61 to 70 year group.

The racial distribution was as expected: 77 Negroes, one Filipina, and one white.

Thirty-three patients were nulliparas; 46 were parous. Sixty patients were not pregnant and nineteen were pregnant at the time of the diagnosis.

TABLE II. DIFFERENTIAL DIAGNOSTIC LABORATORY TESTS USED

1. Dark-field examination (*Treponema pallidium* and fusospirochetes)
2. Serologic tests for syphilis
3. Ducrey bacillary skin test (chancroidal infection)
4. Direct smear, Gram's stain (*Hemophilus ducreyii*)
5. Culture for *Hemophilus ducreyii*
6. Biopsy for: (a) malignancy (b) condyloma acuminatum (c) tuberculosis (d) mycotic infections (e) tissue type (f) granuloma inguinale
7. Frei test
8. Frei test biopsy
9. Smear type biopsy for granuloma inguinale (superior)
10. Smears for inclusion bodies (herpes progenitalis)
11. Rabbit inoculation, eye (herpes progenitalis)
12. Guinea pig inoculation (*Mycobacterium tuberculosis*)
13. Culture for *Mycobacterium tuberculosis*
14. Tuberculin tests
15. Direct examination of material for fungi (*Actinomyces, Blastomyces, Candida*)
16. Fungus and bacterial cultures

A "sore on the privates," abdominal and pelvic pain, fever, a purulent or bloody vaginal discharge were the chief complaints for which the patients sought relief. The duration of symptoms varied from four days to fourteen years.

The lesions were limited to the vulva in 47 of the 79 patients. Ulcerations were present on the vulva and in the vagina in 9; vulva and inguinal regions in 4; vulva and cervix in 2; vulva and mouth in one. In 4, the lesions were limited to the vagina; in 2 to the vagina and inguinal regions. Six patients had the process limited to the cervix; one had cervical and abdominal involvement; one had cervical and questionable abdominal involvement; one had left inguinal lesions only, and one had the lesion on the buttocks.

Treatment

Seventy-two of the 79 patients were treated in the era when antimony compounds were considered specific in granuloma inguinale. Tartar emetic (1 per cent) given intravenously two to three times weekly in increasing doses was preferred to Fuadin. Our experience with tartar emetic was not entirely satisfactory. The treatment was prolonged and many patients failed to continue with the therapy. Patients also failed to respond and the recurrence rate was high. Local therapy in an effort to clear up secondary infection was advised in every patient.

Eleven patients, who had elephantiasic enlargement of the vulva, had simple total vulvectomy and intensive tartar emetic therapy. Three patients had a partial vulvectomy done twice.

One patient had exploratory laparotomy. Her case history is presented in detail.

Only one of the nineteen pregnant patients had a cesarean section and this was done for primary uterine inertia and not because of the granuloma inguinale.

The last seven patients seen have been treated with streptomycin with complete success. The patients were hospitalized and given 1 Gm. of streptomycin intramuscularly every six hours for five days with an average total

dose of 20 Gm. In contrast to the response to the antimony compounds, the response of the lesions to streptomycin was dramatic. Healing was complete in from one to five weeks depending upon the extent of the lesions. No patient has had a recurrence following streptomycin therapy.

Recent reports[6] indicate that aureomycin and Chloromycetin are equally effective but we have had no experience with these antibiotics in treating granuloma inguinale.

Mortality

Two of the 79 patients died, a mortality of 2.5 per cent. One in the early years had a pelvic examination under anesthesia because of profuse hemorrhage. She aspirated vomitus and died.

The second patient had an exploratory laparotomy. The diagnosis of granuloma inguinale of the tubes, ovaries, pelvic peritoneum, and retroperitoneal tissues was confirmed by biopsy.

These deaths make it obvious that granuloma inguinale can be a very serious and hazardous disease. The obvious maternal hazards of infection and hemorrhage in granuloma inguinale complicated by pregnancy have been repeatedly reported. Case 2 shows the danger of the infection following a spontaneous delivery.

CASE 1.—L. G., a 28-year-old Negro woman, para vi-i-iii, was admitted to the hospital on April 17, 1942, complaining of constant left lower abdominal pain, intermittent fever and chills, nausea, loss of forty pounds in weight, and amenorrhea of four months' duration. She stated that prior to Oct. 1, 1941, she had always enjoyed good health. She had been seen by a physician shortly after the onset of her illness who told her that she had "ulcers on the mouth of the womb and bad blood." Apparently this physician cauterized the cervix and during the next ten weeks gave her weekly intravenous injections. This intravenous therapy was thought to be some arsenical preparation for syphilis. Because of her progressive chronic illness and failure to improve she went to another physician on April 15, 1942. He referred her to us with a diagnosis of carcinoma of the cervix. Interestingly, the first examiner in our clinic made the diagnosis of Stage III carcinoma of the cervix.

Examination showed a chronically and acutely ill, well-developed, emaciated Negro woman. Her temperature was 39.6°; pulse 120; respirations, 20; blood pressure 106/65. The abdomen showed a mild lower abdominal distention. In the left lower quadrant there was an oval-shaped 6-cm. mass extending from the iliac crest down to the symphysis pubis. The mass was only slightly tender but was firm and immobile. There were no other palpable masses. The superficial inguinal lymph nodes were palpable bilaterally but were not tender. Pelvic examination revealed normal external genitals and moderate relaxation of the pelvic floor. Vaginal walls were smooth and clean and the mucosa was intact. The cervix was covered with a dirty, beefy-red, nodular but soft lesion. It did not bleed readily to touch. There was no surrounding infiltration as the fingers easily encircled the cervix. The uterus could not be outlined. On the left there was a large indurated fixed mass apparently not connected with the cervix but filling completely the left half of the pelvis to the lateral pelvic wall. The mass was only moderately tender. The right side of the pelvis was relatively clear. Rectal examination showed a constriction of the rectum at the depth of 8 cm. which was thought to be due to pressure from the mass. The accessory clinical findings revealed hemoglobin of 50 per cent; red blood cells 2,000,000; white blood cells 16,000. The urine showed a trace of albumin, 10 to 12 white blood cells, rare red blood cells, and granular cast. Blood serology tests were positive. A flat plate of the abdomen was negative. A biologic pregnancy test was negative. X-rays of chest were negative. Barium enema showed the mid-portion of the rectal ampulla to be slightly narrowed, spastic, and irregular. The sigmoid and rectosigmoid were displaced upward and to the right by the mass in the left lower quadrant. A biopsy of the cervix revealed Donovan bodies in the cytoplasm of the mononuclear cells. The Frei test was negative. The Ducrey bacillus skin test was negative.

The patient's temperature ranged from 37 to 39° C. daily for the first seven days and then from 37 to 38° C. for the next six days. During this time she was treated with daily transfusions and intravenous tartar emetic. On April 29, 1942, an exploratory laparotomy was done as the patient was not responding to the conservative therapy and it was thought that she might have left ovarian abscess. Examination of the pelvis revealed a normal uterus, the right tube and ovary showed a minimal inflammatory reaction; there were 150 c.c. of straw-colored fluid in the pelvis. The left tube and ovary were involved in a mass of grayish-yellow granulomatous tissue. A biopsy of this mass was done, as was a biopsy of the retroperitoneal tissue lateral to the base of the left infundibulopelvic ligament. These biopsies revealed Donovan bodies. In spite of intravenous tartar emetic, transfusions, etc., the patient died on May 17, 1942, one month after admission to the hospital and eighteen days after operation. A necropsy was done and the final anatomical diagnosis was granuloma inguinale of cervix, retroperitoneal tissues, pelvic peritoneum, and ovaries; dense fibrosis of pelvic retroperitoneal tissue; fixation of rectum; perforation of rectum; acute generalized peritonitis; focal necrosis of liver; chronic pyelonephritis and hydropericardium.

CASE 2.—R. W., a 27-year-old Negro woman, a nullipara, was first seen on Aug. 8, 1945, complaining of progressive ulcerations of the vulva of twenty-two months' duration. The initial lesion was a small lump at the left fourchette first noted in November of 1943. This became very painful, increased in size, "broke down," and drained a thin clear fluid. In February, 1944, she went to a venereal clinic and blood serology tests were done. She stated that no pelvic examination was made. She was told that she had a doubtful Wassermann test and she was started on weekly intravenous and hip injections which were continued for seven months. This seemed to have no beneficial effect and the process extended to involve the entire labia, perineum, left buttock, and perirectal area. The lesion began to drain a dark-red foul fluid and itching became a predominant symptom. Pelvic examination revealed the mons veneris and upper labia to show a brawny induration. The lower labia, perineum, left buttock, and perianal areas were involved in an extensive serpiginous ulceration. There was marked vaginal stenosis which would not permit one-finger examination due to pain. There was such stricturing of the rectum that a rectal examination could not be done. Tissue smears made from the lesions showed numerous Donovan bodies. The blood serology tests were doubtful; the Frei test was positive. She was started on intravenous tartar emetic and was sent to her local physician for continuation of the therapy.

She was next seen on Aug. 14, 1946, one year after her initial visit. She had been receiving regular antimony therapy the entire time. The lesion was the same and she was three months pregnant. The rectal stricture had cleared. She was continued on antimony intravenously and was admitted to the hospital on Feb. 23, 1947, in active labor. She had a rapid labor and was spontaneously delivered of a normal living female infant without episiotomy and no laceration was sustained. On the day of delivery her temperature spiked to 38.5° C. She developed a generalized peritonitis with adynamic ileus and anuria, and was quite ill for twenty days. She was finally discharged on the twenty-eighth day. A subsequent check in October of 1947 revealed an elephantiasic enlargement of the labia and granulomatous tissue still present at the fourchette, on the perineum and left buttock. She was admitted to the hospital on Oct. 21, 1947, for vulvectomy and streptomycin therapy. The vulvectomy was performed on Oct. 24, 1947. The microscopic examination revealed granulomatous tissue but no Donovan bodies. She was given 42 Gm. of streptomycin over a period of fourteen days. She was last seen in December of 1947 at which time the vulva, perineum, and left buttock were completely healed.

Summary

1. Seventy-nine women patients with granuloma inguinale were observed at Duke Hospital during a nineteen-year period ending Jan. 1, 1950. It is

certain that this was not the true incidence. Seventy-seven patients were Negroes, one was white, and one was a Filipina.

2. The etiology, the diagnosis, the differential diagnosis, the symptomatology and treatment of these patients have been critically reviewed.

3. The recognition and differential diagnosis of vulvar lesions requires a definite diagnostic routine and close cooperation between the clinician, pathologist, and bacteriologist.

4. The use of antibiotics as a specific should replace antimony compounds in the treatment of granuloma inguinale. Early diagnosis is always important.

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Discussion

DR. CONRAD G. COLLINS, New Orleans, La.—Dr. Thomas has admirably presented the difficulties associated in the specific diagnosis of hyperplastic, hypertrophic, and/or ulcerative lesions of the vulva. He has repeatedly emphasized that the clinical appearance, visual and palpatory, of these lesions, though supplying a clue to the identity of the specific etiological agent, is exceedingly likely to lead one into error. Stress has been laid upon the fact that a combination of various diseases in the same patient is not uncommon. The justifiable, logical, and indispensable conclusion was reached that the recognition and differential diagnosis of vulval lesions requires a definite diagnostic routine and close cooperation between the clinician, pathologist, and bacteriologist. Now that laboratory methods not only allow for accurate specific diagnosis in these cases, but are indispensable, it has for years been fundamental on the gynecologic and obstetric services at Tulane University that no therapy be applied in these cases until a diagnosis has been precisely formulated. It is not only important to know what etiological agent is present, but it is of the utmost importance that we be certain that no other determinant of hyperplastic, hypertrophic, and/or ulcerative lesion exists. Thus a positive laboratory test for one etiological agent should not obviate completion of the diagnostic routine so well described by Dr. Thomas. Biopsy, smears for Donovan bodies and Ducrey's bacillus, the Frei test, darkfield examination and serologic test for syphilis constitute a minimal diagnostic survey. Syphilis, granuloma inguinale, lymphopathia venereum, and chancroidal disease all produce hyperplastic and hypertrophic lesions indistinguishable microscopically. It is not surprising then that of 37 biopsies from patients having granuloma inguinale of the vulva submitted to the pathologist only 9 were returned with positive diagnoses of granuloma inguinale. Some claim that by special silver stains tissue diagnosis of granuloma inguinale can be effected; we, however, rely solely upon examination of smears.

Biopsy effectively establishes the presence or absence of carcinoma or tuberculosis. We have not found it necessary to utilize guinea pig inoculation or cultural methods for diagnosis of the latter. We have not observed any cases of actinomycosis or blastomycosis of the vulva.

Antibiotics have replaced tartar emetic in the therapy of granuloma inguinale. Streptomycin is the antibiotic of choice at present and in our clinic the results parallel those found at Duke University.

Fourteen of the author's 79 patients were submitted to vulvectomy. We believe that hyperplastic or hypertrophic lesions of the vulva irrespective of the etiological agent predispose to the development of vulval carcinoma.

Of 30 cases of carcinoma of the vulva observed and treated by us since Jan. 1, 1946, 7 were associated with hypertrophic or hyperplastic lesions. Of these hyperplastic lesions 4 were due to syphilis, 2 to granuloma inguinale, and 1 to a mixed chancroidal and lympho-granuloma venereum infection.

On our service unless there is complete return of the involved tissues to normal following chemotherapy and/or antibiotic therapy, total radical vulvectomy is performed. We prefer total radical vulvectomy as we believe that blood loss is smaller, postoperative discomfort diminished and the end result both functional and cosmetic better, than if simple or partial vulvectomy is utilized.

The characteristics of the inguinal nodes are of no more aid in diagnosis than are the clinical features of the vulval lesions and though much has been written regarding the differential diagnosis of vulval lesions based upon inspection and palpation, the only determinant is the laboratory.

Fortunately, these similar pathologic processes attack areas easily accessible to gross and microscopic study. Errors in diagnosis should be exceedingly rare if studies as outlined by Dr. Thomas are carried out in each and every case.

DR. JOHN PARKS, Washington, D. C.—Dr. Thomas has presented an impressive series of 772 patients with ulcerative lesions of the external genitals studied in the Duke University Gynecological Clinic. He has elected to focus our attention on granuloma inguinale. This is a timely paper in that the two essentials in the management of any disease, namely, (1) a method of diagnosis, and (2) specific treatment, are now available for granuloma inguinale. It has been our experience, too, that the direct fresh tissue smear biopsy is a far more reliable method of demonstrating Donovan bodies than is the usual fixed tissue slide. In therapy, streptomycin and Chloromycetin have proved to be far more specific than tartar emetic or Fuadin. The sulfonamides and antibiotics have so altered the clinical course of many diseases that the full pathologic sequences of certain infections are seldom available for clinical study. Granuloma inguinale recently has come under this category. Now that it is possible to make a definite diagnosis and give specific therapy, some of the unknowns in epidemiology and additional details regarding tissue dissemination of granuloma inguinale will have to evolve through scientific curiosity rather than medical necessity. There are several points in Dr. Thomas' paper which justify re-emphasis. Multiple infections causing ulceration of the vulva are common. A systematic survey, as advocated, is essential for an accurate differential diagnosis. Moisture, warmth, trauma, and constant contamination of this anatomical area predispose all ulcerative lesions of the vulva to secondary infection. Distortion of lesions by secondary infection often makes a definite diagnosis difficult. An example of granuloma inguinale with associated secondary infection, avitaminosis, and fusospirochetosis is illustrated by a patient from our Gallinger Municipal Hospital Service. The primary diagnosis was made by fresh tissue smear. Medical treatment and minor plastic surgery, carried out in the healing phase of the disease, resulted in a clinical cure. Pigmentation was absent in the regenerated skin, indicating that the full thickness of the epithelium was destroyed by the disease. Granuloma inguinale, like syphilis, destroys nerve endings in the dermis. Unless secondarily infected, granuloma inguinale is a painless disease. There was a tremendous hypertrophy of the vulva with ulceration due to granuloma inguinale, yet the patient had no pain. Her only complaint was the inability to wear a bathing suit. Dr. Thomas has suggested that granuloma inguinale may become a generalized disease. Extragenital lesions, as illustrated by a patient with granuloma inguinale involving the vulva, soft palate, and cheek, indicate a systemic dissemination of the infection. Finally, the patient with chronic granuloma inguinale sems to have some increased predisposition to squamous-cell carcinoma. In addition to the initial diagnostic biopsy, repeated biopsies should be taken of all ulcerative lesions which fail to respond to specific medical treatment.

DR. LESTER A. WILSON, Charleston, S. C.—We have employed streptomycin therapy in the treatment of 35 cases of granuloma inguinale during the past two years with

excellent results.   It is too early at this time to be certain of cures; however, we have
had no recurrences.

About thirty years ago, I reported 14 cases of labor complicated by granuloma in-
guinale, and at that time it was my opinion that vaginal delivery without any pelvic
examination was preferable.   My experience since has confirmed this earlier opinion.

In our series of cases, we have not found any husband or partner who was infected
with the disease.   As a result, we are led to believe that it is not venereal.   Furthermore,
we have found no increase in the incidence of abortions, premature delivery, nor sterility
in individuals who have granuloma inguinale.

It is intriguing to think how these women, with their multitude of lesions, manage
to get pregnant even once, no less than to do so repeatedly.

DR. THOMAS (Closing).—I do not agree with Dr. Collins that a radical vulvectomy
is necessary for this disease.   Perhaps he is a much better plastic surgeon than we are.

I would emphasize that great progress has been made in the diagnosis and manage-
ment of this disease during the past few years.   Prior to this, granuloma inguinale was a
scourge.   We have, in the newer antibiotics, a specific therapy.   Interestingly, since we
have this adequate therapy, we are seeing fewer patients with the disease.

INDUCTION OF LABOR*

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THE subject of induction of labor has undergone evolutionary changes in the past few decades. In the early days, it was undertaken chiefly to produce premature birth of a baby when it was known that there was a contracted pelvis.

With the perfection of surgical technique and, more recently, the protection afforded by the use of antibiotics, the safety of induction, even as an elective procedure, has been greatly enhanced.

I am about to present my results in a series of inductions, chiefly elective in nature, by a very simple method, that of stripping and rupturing the membranes. As will be emphasized later, the case must be suitable for the procedure, and if so it gives excellent results.

Choice of Patients for Induction

It is my firm conviction that, in the practice of good obstetrics, we are serving our patients better by the judicious use of elective inductions in patients who show they are ready to deliver, i.e., when the cervix is "ripe," beginning to dilate, and the presenting part is well engaged.

With this in mind, I very cautiously began to induce labor in private patients ten years ago, and since then I have induced it in approximately 600 cases, but for the purpose of this report, I am summarizing the 455 inductions by stripping and rupturing of the membranes.

Thirteen of our patients had toxemia of pregnancy, one had malignant hypertension, one oligohydramnios, two marginal placenta previa, one diabetes, one polyhydramnios, and there were three pairs of twins. All of the rest were chosen as suitable because they were at or near full term, the presenting part thoroughly engaged, and the cervix soft and partially dilated and without disproportion. The ideal cases were those in which the cervix was thinned out and anterior, as well as partially dilated.

During the same period of time, there were at least 150 patients who started in labor after the administration of castor oil. Furthermore, any patients actually in labor, in whom the membranes were ruptured to expedite the labor, are not considered.

Method of Induction

Our very simple method of induction consists of having the patient come to the hospital between eight and nine o'clock in the morning, after a breakfast consisting of fruit juice and a cup of tea or coffee: She is given the usual

preparation consisting of soapsuds enema and local preparation, after which
she is given a hypodermic of morphine sulphate, ⅙ grain, or Demerol, 100 mg.,
with scopolamine, ⅟₁₅₀ grain, 45 minutes later scopolamine, ⅟₂₀₀ grain, and at
the end of the hour the patient is scrubbed for internal examination.

No anesthesia is ever necessary; the vulva is painted with aqueous Mer-
thiolate and about an ounce of the same substance instilled in the vagina.

Two fingers are then introduced into the vagina, the cervix stretched
gently, the membranes stripped, and allowed to bulge through the external os.
The membranes are then ruptured with an Allis forceps and the presenting
part displaced upward slightly, so as to permit the escape of a considerable
quantity of amniotic fluid. This procedure has never caused prolapse of the
cord. An accurate notation of the position of the presenting part is made,
and the fetal heart then carefully checked, so as to be sure that the induction
has caused no embarrassment to the fetal circulation.

TABLE I. DILATATION AT INDUCTION

	FINGERBREADTHS	PATIENTS	PER CENT
Primigravidas.—			
	1	14	12.7
	1½	14	12.7
	2	73	66.4
	3	7	6.3
	4	2	1.8
Multigravidas.—			
	1	10	2.9
	1½	20	5.8
	2	180	52.2
	3	87	25.5
	4	42	12.2
	5	6	1.7

Referring to Table I, more than half of the patients showed a dilatation
of two fingerbreadths at the time of the induction. In the primigravida, the
amount of thinning of the cervix was considered more important than in the
multigravida. It was interesting to note that 87 of the multigravidas (25
per cent of them) were three fingerbreadths dilated without labor having
begun, and 42 multigravidas and 2 primigravidas were four fingerbreadths
dilated. In 6 instances, multigravidas were five fingerbreadths or more dilated
without any evidence of onset of labor.

These figures seem significant and one wonders if the importance of rou-
tine rectal examinations on all patients approaching full term has been suf-
ficiently emphasized.

TABLE II. METHOD OF DELIVERY

METHOD	PATIENTS	PER CENT
Low forceps	160	35.1
Low mid forceps	192	42.2
Mid forceps	72	15.8
Podalic version	11	2.4
Breech extraction	7	1.5
Spontaneous	11	2.4
Craniotomy	1	0.22
Cesarean	1	0.22
Total	455	

As is the custom in our clinic, most of our patients were delivered by low,
low mid, or midforceps, and, among these, there were 43 modified Scanzoni
maneuvers performed on persistent posterior presentations. Podalic version

was utilized in 11 instances, in addition to the versions on the second of 3 twin pregnancies, and there were 7 breech presentations delivered as such. There was 1 cesarean section in a multigravida, who had had one previous stillborn baby. The head was engaged and the cervix was three fingerbreadths dilated. She was given 6 hours of active labor after the induction without progress and a transverse laparotrachelotomy was then performed, the diagnosis being moderate cephalopelvic disproportion.

One macerated erythroblastotic baby who had died in utero several days before induction was delivered by craniotomy.

TABLE III. LENGTH OF LABOR, PRIMIGRAVIDAS

TIME (HOURS)	PATIENTS	PER CENT
2	7	6.4
3	6	5.4
4	10	9.09
5	15	13.6
6	13	11.8
7	14	12.7
8	13	11.8
9-11	17	15.5
12-20	11	10.0
20-33	4	3.6
Total	110	

Labor was appreciably shortened from the averages which have been quoted in our textbooks and you will note by referring to Tables III and IV that 94 (or 86 per cent) of the primigravidas delivered within 11 hours, and 338 (or 97 per cent) of the multigravidas delivered within that length of time. Moreover, 287 (or 83 per cent) of the multigravidas delivered within 6 hours. The average length of labor for the primigravidas was 7 hours and 54 minutes, and the average for the multigravidas was 4 hours and 30 minutes. These figures are quite astonishing but, I assure you, are true.

TABLE IV. LENGTH OF LABOR, MULTIGRAVIDAS

TIME (HOURS)	PATIENTS	PER CENT
Less than 1	3	0.9
1	18	5.2
2	56	16.2
3	75	21.7
4	55	14.5
5	43	12.7
6	36	10.4
7	21	6.9
8	14	4.0
9-11	16	4.6
12-20	7	2.0
21	1	0.3
Total	345	

Analgesia and Anesthesia

There has been a gradual evolution of our methods of obtaining analgesia during labor as well as our means of administering anesthesia for deliveries during this ten-year period.

During the first six years of the time, we used morphine and scopolamine for primigravidas, and barbiturates, usually Sodium Amytal or Seconal, for

multigravidas during labor. All deliveries were performed under ether or
N20-ether anesthesia.

In the past few years, however, we have used Demerol-scopolamine anal-
gesia for almost all cases, and in the past two years most of our deliveries
have been under saddle-block anesthesia, with the use of 5 mg. of Pontocaine
Hydrochloride, intrathecally, weighted with 2 c.c. of 10 per cent glucose.

Episiotomy has been employed routinely in practically all of our cases.

TABLE V. LATENT PERIOD, PRIMIGRAVIDAS

LENGTH OF TIME	PATIENTS	PER CENT
30 minutes or less	14	12.7
Within 1 hour	16	14.5
2 hours	20	18.2
3 hours	14	12.7
4 hours	11	10.0
5 hours	15	13.6
6 hours	4	3.63
7 hours	7	6.4
8-11 hours	3	2.73
12-20 hours	3	2.73
21-27 hours	3	2.73
Total	110	

The interval between the stripping and rupturing of the membranes and
the onset of labor varied greatly. However, 45 per cent of the primigravidas
and 60 per cent of the multigravidas were in active labor within two hours,
and 88 per cent of all were in active labor within five hours (Tables V and VI).

TABLE VI. LATENT PERIOD, MULTIGRAVIDAS

LENGTH OF TIME	PATIENTS	PER CENT
None	19	5.5
30 minutes or less	65	18.8
Within 1 hour	67	19.4
2 hours	59	17.1
3 hours	46	13.3
4 hours	27	7.8
5 hours	27	7.8
6 hours	11	3.2
7 hours	6	1.7
8-11 hours	10	2.9
12-20 hours	4	1.13
21-27 hours	4	1.13
Total	345	

It should be noted that there was no latent period in 19 of the multi-
gravidas while 30 of the primigravidas and 132 of the multigravidas, or 40 per
cent of the total, were in labor within one hour. The average latent period
among the primigravidas was four hours and, for the multigravidas, two
hours and forty-eight minutes.

Incidental Surgery

At the time of delivery, various incidental surgical procedures were some-
times considered advisable. The most common was that of external hemor-
rhoidectomy, especially in cases where there were large thrombosed piles.
This was carried out in 36 instances (0.8 per cent). There were also 12 in

which secondary perineorrhaphy was performed. The other procedures consisted of the occasional excision of moles, and cysts, and, in a few instances, trachelorrhaphy and/or urethroplasty was done.

There was maternal morbidity in 14 cases, 10 of which were due to retention of lochia, 2 to pyelitis, 2 to cystitis (3.07 per cent), and there were no maternal deaths.

Summary

In a series of 455 cases of induction, 435 of which were elective, there was no maternal mortality, a maternal morbidity of 3.07 per cent, and a fetal mortality of 2 per cent, corrected to 0.2 per cent.

TABLE VII. RESULTS

	PATIENTS	PER CENT
Mothers discharged well	455	100
Mothers discharged dead	0	0
Total babies delivered (3 sets of twins)	458	
Babies discharged well	448	98
Babies discharged dead	10	2
Corrected fetal mortality	1	0.2

TABLE VIII. FETAL DEATHS

1. *Stillbirths.—*
   3 Erythroblastosis
   1 Diabetes, dead 10 days
   1 Toxemia, dead 4 days

2. *Monstrosities at Term.—*
   1 Congenital intestinal obstruction
   1 Multiple anomalies
   1 Spina bifida (lived 7 days)

3. *Intrapartum Deaths.—*
   1 Four loops of cord around neck

4. *Prematurity.—*
   1 Severe toxemia

It is our firm conviction that in the art of obstetrics we are serving our patients as they should be served by inducing labor in those who are at full term and who show by examination that the cervix is ripe, and dilatation has begun, providing that the presenting part is thoroughly engaged in the pelvis and there is no evidence of disproportion.

Labor is definitely shortened and the results are most gratifying, because the patient enters the hospital properly prepared for parturition. I am not advocating routine inductions, but am convinced that simple stripping and rupturing of the membranes is an adequate method of choice in properly selected cases.

10515 CARNEGIE AVENUE.

Discussion

DR. H. CLOSE HESSELTINE, Chicago, Ill.—Dr. Reycraft is to be commended for his straight-forward presentation. Obviously, he or anyone else may expect criticism for the performance of a procedure which is not in common practice or is a digression from

policies not in vogue by the majority of eminent obstetricians in the United States. Yet, before one offers criticism, one must recognize that progress is made only by explorations into new fields as well as the reinvestigations of previously rejected areas. Some of the previously tried and discarded practices might, with refinements and improvements in techniques and therapies, become not only safe but desirable.

Progress means that we must, by necessity, evaluate our present procedures and investigate new possibilities. A change, to be acceptable, must at least offer an equal safety to the mother and to the child as compared to the standard and accepted procedure; and in addition, an innovation must convey extra benefits if there is not the reward of an increased safety factor due to the new procedure itself.

As Dr. Reycraft has indicated, many aspects of obstetrics have remained comparatively unchanged. For instance, there is not a satisfactory control for or a deferment of the onset of labor for an arbitrarily set time. In our experience there is not a completely reliable method of induction of a normal labor for an arbitrarily selected date. Dieckmann found a definite latent period after rupture of membranes in those presumably susceptible to induction.

Dieckmann, Davis, and I have been interested in the feasibility and practical application of selective inductions of labor for reasons other than medical, such as Dr. Reycraft has suggested. Surely, no one would object to convenience to the obstetrician if it can be accomplished without jeopardy or hazard to the mother or the baby. Castor oil and quinine have been discarded in the Chicago Lying-in Hospital routine for induction. Likewise, bags, bougies and other mechanical contrivances have carried risks with them.

By doing sufficiently frequent vaginal examinations, Dieckmann has gained the impression that the cervix is relatively uneffaced at 6 weeks, about half effaced at 4 weeks, and is effaced at 2 weeks before spontaneous full-term labor, in the primigravida. The condition in the multipara is somewhat similar except the cervix is slightly thicker. In exceptional instances effacement and dilatation may occur well in advance of calculated date of delivery. We do vaginal examinations in the office on selected patients to determine when the cervix is "ripe." In some with complete effacement, slight dilatation, and a "ripe" cervix labor may be induced by "rimming the cervix" or "stripping of the membranes" but without rupture of membranes. This policy has applied to patients who have rapid labors, live at a great distance from the institution, and have poor transportation facilities, or for other reasons in which it might be desirable and convenient to have the onset of labor planned by schedule. Vaginal examinations may alter the bacterial flora of the vagina or introduce organisms into the cervix to the extent that the morbidity rate may be increased. Certainly a cesarean section would be associated with increased risk, the degree of which cannot be determined, after the first day up to the sixth or seventh day after such an examination.

We have found that the so-called "stripping" of the membranes and "rimming" of the cervix not infrequently will bring on labor. Some medical or obstetrical complications may necessitate the induction of labor. In this event one may rupture membranes and follow this with hypodermic injections of solutions of minute but graduated amounts of posterior pituitary extract. However, this is digression from the tenet of Dr. Reycraft's presentation.

Dieckmann's series of 165 cases of induced labor indicate the results for a three-year period. During this time there were over 12,000 deliveries. Many of these inductions were for medical or obstetrical indication which explains in part the high stillbirth and neonatal death rate. The one maternal death was not the result of induced labor but of a complication which indicated the rupture of the "bag of waters." Dr. Reycraft's 2 per cent gross fetal mortality is somewhat high. Although I agree with Dr. Reycraft's desire for a more complete understanding and application of inductions of labor, it would be definitely unwise to urge it upon the general practitioners and even upon the obstetricians until better safeguards and more clear-cut definitions for the fulfillment of conditions for its application, lest it contribute to an increased maternal and fetal morbidity and mor-

tality. Certainly, if labor did poorly, and it may under the influence of attempted induction, and abdominal delivery became necessary, there might be an increased hazard of infection. Moreover, we must make sure that the unborn child is in no way jeopardized. If there is any alteration in the opportunities of life, birth, and subsequent good health, that principle must be directed toward a safer course. Those who are fundamentally interested in this direction and have facilities (clinical and other) may be justified in the exploration only as long as the investigators keep the experiment controlled and also abide by the code of experimentation upon pregnant women.

DR. MELVIN A. ROBLEE, St. Louis, Mo.—Dr. Reycraft has presented a most interesting report of 455 selected cases, hand picked for induction out of some 600 cases induced by him. In all but 20 of these there were no obstetrical indications. Little or no morbidity was shown.

In order to show the morbidity of induced labor we should not confine our reports to personal experiences of a single expert who strips and ruptures the membranes of patients already passing through the threshold of labor, but review its uses in so-called obstetrical indications as practiced by several different obstetricians who seek to extend its application in solving obstetrical problems.

If we do this over a period of years the conclusions reached are: Induction of labor has little or no obstetrical usage except in the management of toxemias, including diabetes and perhaps a few cases of erythroblastosis; little or no use in the postmature cases; little or no use in the management of cephalopelvic disproportion.

In fact, labor cannot be induced without some degree of combined morbidity except within 48 hours of the time spontaneous labor would have started anyway.

Furthermore, in studies limited to degrees of morbidity, the more morbid patients are those with longer hours of labor, to produce babies of lower than average birth weight, whereas the less morbid patients have shorter hours of labor to produce babies of average or above average birth weights.

This means that only in the mature cases prepared for labor with effaced dilated cervices can labor safely be induced. If labor does not follow rupture of the membranes within 12 hours it is better to institute bed rest, adequate food and fluids, and the use of antibiotics than to force labor with oxytocics. Sometimes 4 to 5 days will intervene before labor starts.

I would like to ask Dr. Reycraft how he managed the few cases which might fail to respond to stripping and rupture of the membranes?

DR. J. BAY JACOBS, Washington, D. C.—I have been inducing labor for many years and I had discussed Dr. Roblee's paper originally. Although he has not changed his views I am not critical of them, since he has some good ideas.

Dr. Reycraft's views are very much in line with mine, and I might say to begin with that his cases were very well selected and the criterion of that opinion is the fact that he encountered very few prolonged labors. Most of his patients delivered within the average length of time, which shows that they were carefully selected. Occasionally a case is improperly selected and it may be some time before the patient starts in labor, or after starting she may have an unduly prolonged labor.

In the induction of labor, I prefer not to incur the risk of disengaging the presenting part and for that reason do not strip the membranes, nor do I endeavor to drain off much amniotic fluid. In cases where there are no forewaters, I have found that the mere scraping of the membranes in an attempt to perforate them will institute uterine contractions even though one might not notice any loss of amniotic fluid. I have never found it necessary to administer Demerol or scopolamine or any other drug or anesthetic for the purpose of rupturing membranes. The procedure is simple to perform and is practically painless. Where there is mechanical difficulty encountered in rupturing the membranes, which might indicate the use of analgesia or anesthesia, it is best not to attempt rupture of membranes, unless there were urgent indication, since prolonged labor with its ill effect would most probably result.

I was impressed with one comment relative to the position of the cervix. If the cervix is located posteriorly and labor is induced, one may anticipate a prolonged labor. However, if the cervix is soft and located anteriorly, labor will begin shortly after the membranes are ruptured, and will be of short duration. The essayist wisely prefers not to induce labor where the cervix is situated posteriorly.

Induction is not performed in many of my patients because of mechanical indication. There are various reasons why the patient or obstetrician might prefer to follow this procedure. When I believe that a patient is at term and that the estimated date of confinement is very close, I might consider induction. I do not perform vaginal examinations in the office late in pregnancy, although I think that Dr. Hesseltine's suggestion is a practical one. For that reason, I find it advisable to discharge from the hospital a certain proportion of my patients, without inducing labor, if the position and condition of the cervix do not appear favorable upon vaginal examination. Of course, the patient is informed of this possibility before she is admitted to the hospital.

Regardless of physical findings, it is highly advisable to pay particular attention to the estimated date of confinement. As an example I wish to quote a very recent experience: A primipara who was not sure of the date of her last menstrual period was referred to me late in pregnancy, and appeared to be at term. On vaginal examination the presenting part was well engaged, the cervical canal was obliterated and the cervix was almost 2 fingers dilated. Although I was to leave town for about 10 days and felt that the patient would start in labor very soon, I did not induce labor because according to the estimation of the referring physician she was not due for 3 more weeks. Labor started spontaneously about 2 days later and she was delivered by another obstetrician of a baby weighing 4 pounds, 12 ounces. The infant happened to have a tracheoesophageal fistula for which he was operated upon and died. If labor had been induced in this case, it would have resulted in embarrassment to me because of the size of the baby, and it is obvious as to what the patient's attitude would have been.

One must be particularly careful in selecting cases for induction as well as in advocating this procedure. Only qualified obstetricians should be permitted to induce labor.

DR. S. A. COSGROVE, Jersey City, N. J.—What is your management in medical indication for induction?

DR. REYCRAFT (Closing).—I really anticipated many more comments and perhaps antagonism to the principles presented. Dr. Roblee asked me what I would do in a case that would not "induce." In the first place, I am not talking about that kind of case right now. I am trying to talk about those I am positive are ready to go. However, in a case (and this more or less answers Dr. Cosgrove) in which for some medical reason labor should be induced, I might still rupture the membranes as a means of starting labor and if the patient was slow in starting because she was not ready to proceed, put her to bed, give her intravenous glucose and other fluids, plenty of nourishing food, and high protein diet, if there is no sign of labor at all. More recently in cases of that type we have been playing with the use of dilute Pituitrin or Pitocin for stimulation of uterine contractions. So far, we have not seen any failures. I should say also that we have not seen any catastrophies. There have been some reported, I am told, although I do not believe they have appeared in the literature as yet. We do not like to use accouchement forcé—we prefer to see if the patients will not deliver themselves in due course of time.

CLINICAL AND ROENTGEN PELVIMETRY: A CORRELATION*

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CONTROVERSY regarding the relative merits of clinical and roentgen pelvimetry has aroused our interest. Divergent opinions exist, from the concept that the x-ray is unnecessary and that clinical pelvimetry is all important, to the teaching that the x-ray is the final answer to all pelvic dystocia problems. At the outset, we would like to agree with Eastman[1] who states that the truth lies somewhere between these two extremes.

We here present a review of our experiences with 200 cases followed in the dystocia clinic of the Department of Obstetrics at the University Hospital. Patients screened from the prenatal clinic who have clinically abnormal pelves, history of previous dystocia, cesarean section, or unexplained stillbirth are examined in the dystocia clinic. There, detailed pelvic estimation is performed and roentgen pelvimetry ordered near term if indicated. At about 38 weeks of pregnancy the patient is examined clinically, her films evaluated and a prelabor estimation chart is completed. Copies of both the clinical pelvimetry record and prelabor estimation chart are filed in the delivery suite for reference during labor and delivery. Following delivery, the patients are again seen in the dystocia clinic for their regular postnatal examination, and at this time each case is reviewed in retrospect and suggestions made for the management of subsequent pregnancies. We have omitted the classical external measurements of the pelvic inlet for several years.

Methods and Material

Roentgen pelvimetry is performed in the x-ray department of the University Hospital, the Walton[2]-McLane[3] isometric method being used. Three films are routinely made, namely; (1) a 14 by 17 inch Bucky anteroposterior film of the abdomen with the patient in the supine position, for general information; (2) an 11 by 14 inch Bucky anteroposterior film at 30 inches from the maternal pelvis with the patient in a semireclining position, the pelvis tilted forward so that the inlet is parallel with the film; and (3) a 14 by 17 inch Bucky lateral film with the patient in the same position as for film number 2, but with a notched metallic centimeter rule upright between her legs, as close to the symphysis pubis as possible. Pelvic diameters are measured directly on the lateral film, but a distortion or false centimeter scale must be used in measuring the diameters on the anteroposterior film, taking into consideration the distance between the film and the top of the table upon which the patient is resting. We have enjoyed the complete cooperation of the X-ray Department under the direction of Dr. Walter L. Kilby.

The 200 cases here presented do not represent consecutive cases seen in the dystocia clinic, but are those which have been studied completely as outlined above, and are otherwise unselected. The patients are originally seen in the obstetrical clinic by members of the attending and house staffs, and are then referred to the dystocia clinic upon indication. We would like to make routine x-ray pelvimetry a part of our study in all primigravidas, but our present facilities do not permit. In many instances the pelvic roentgenograms are interpreted by the x-ray department house staff as a part of their training. Patients are evaluated clinically in the dystocia clinic by members of the attending staff who are especially interested in pelvimetry, and members of the house staff are present as often as possible. Thus, house officers of both the obstetrical and x-ray departments participate in this teaching program, with the obstetrical house officers learning to read and interpret roentgen pelvimetry films, and applying this knowledge to clinical obstetrics when they follow these patients in labor and deliver them. After the initial visit of the patient, when the original clinical pelvic estimation chart is completed, all the remaining studies at subsequent visits are made by the group present in the manner of an informal conference. We have found this method most stimulating and mutually instructive. All patients were delivered in the University Hospital by members of the house staff.

TABLE I. UNCORRECTED FETAL MORTALITY ALL IN TERM BABIES

Stillbirths	3	
Death in utero 1 week before labor	1	
Forceps, shoulder dystocia, anoxia	1	
Forceps, atelectasis only	1	
Neonatal deaths	2	
Forceps, intracranial hemorrhage	1	
Spontaneous, atelectasis only	1	
Total fetal mortality	5	2.5%

TABLE II. MATERNAL MORBIDITY AND COMPLICATIONS

Maternal Morbidity.—		
Endometritis, puerperal	18	
Pyelonephritis and cystitis, puerperal	5	
Pneumonia, postoperative	2	
Perineum, cellulitis of, acute	2	
Ileus, adynamic, postoperative	1	
Infection, intrapartum	1	
Total	29	14.5%
Maternal Complications.—		
Perineum, laceration of complete	14	
Preeclampsia, severe	4	
Rh negative, no antibodies	3	
Hemorrhage, postpartum (500 c.c. or more)	2	
Erythema multiforme	1	
Tuberculosis, pulmonary, arrested	1	
Cardiovascular disease, rheumatic, Grade I.	1	
Total	26	

There were 25 white and 175 Negro patients, 150 primigravidas and 50 multigravidas. There were no maternal deaths; and there was an uncorrected fetal mortality of 5 or 2.5 per cent (Table I). The maternal morbidity rate was 14.5 per cent (Table II). Table II also shows maternal complications, of which there were 14 complete perineal lacerations. This is a high incidence of this complication in a series of 200 cases. However, it should be remembered

that all of these patients were delivered by house officers in the process of training, and that many of these patients had contracted pelves. All lacerations were repaired immediately and healed per primam without complication.

Definitions

In order to facilitate an understanding of the various concepts in this paper, which include clinic policy in many instances, the following definitions are given here and the terms are not further defined in the text. Normal pelves are those with Mengert[4] indices for inlet and midplane greater than 125 and 105, respectively. Contracted pelves are those with Mengert[4] indices for inlet and midplane of 125 and 105 or less. Normal deliveries are spontaneous or elective outlet forceps deliveries, while necessary operative deliveries include all other types of deliveries and represent the group in which dystocia is said to have occurred. Prolonged labor is actual labor lasting 24 or more hours. Prolonged second stage of labor is that condition in which complete cervical dilatation has existed for 2 or more hours, and is taken, along with other factors, as indication for operative delivery. A premature baby is one weighing less than 2,500 grams at birth. Extraperitoneal section usually means one of the Norton type, and in this series this operation was frequently done for teaching purposes and not for actual indication.

Reasons for Referral of Patients to Dystocia Clinic

Table III shows the reasons why patients were referred to the dystocia clinic. The patients comprising the major group, 162, were referred because their pelves had been classified as contracted at original clinical examination. That the diagnosis of contracted pelvis is made clinically more often than it is present, a concept pointed out by Groskloss, Robbins and Moehn,[5] is substantiated by our data. Of the 162 patients referred because of clinically contracted pelves, only 79, or 42.5 per cent, were found by study of the x-ray films to have contracted pelves (Table IV). Of the 42 patients with inlet contraction only 18, or 42.8 per cent, had dystocia. Of the 19 patients having midplane and inlet contraction together, 10, or 52.6 per cent had dystocia. There were 18 patients with midplane contraction only, and 12, or 66.6 per cent, had dystocia. However, a total of 37 patients had midplane contraction, and of these, 23, or 62.1 per cent, had dystocia. (See also Table XII.) Therefore, the significance of the midplane as a factor in dystocia is emphasized, and is in agreement with the findings of Eller and Mengert.[6]

TABLE III.   REASON FOR REFERRAL TO DYSTOCIA CLINIC

Clinically contracted pelvis	162
Previous cesarean section	16
History of previous dystocia	14
History of previous stillbirth	2
Breech in primigravida	2
Dystocia dystrophia syndrome	1
Elderly primigravida	1
Long period involuntary sterility	1
Primigravida with floating head at term	1
Total	200

Types of Pelves Encountered

Since the Caldwell-Moloy[7] classification seemed to us to be the most practicable, pelves were tabulated morphologically according to this method, in

the four major groups, depending upon their predominant architecture as determined from our x-ray study. Table V shows the frequency of the types of pelves together with the percentage of normal and necessary operative delivery. It will be seen that in the android type operative deliveries were necessary in 55.31 per cent; and in the platypelloid type an equal incidence of normal and operative deliveries occurred. In both the gynecoid and anthropoid types, normal delivery occurred more frequently than operative.

TABLE IV. CONTRACTED PELVES FOUND RADIOLOGICALLY IN 162 PATIENTS REFERRED
BECAUSE OF CLINICALLY CONTRACTED PELVES

Contracted pelves (x-ray)		79	42.5%
Contracted inlet only	42		
Dystocia	18		42.8%
Contracted midplane and inlet	19		
Dystocia	10		52.6%
Contracted midplane only	18		
Dystocia	12		66.6%
Contracted midplane, total	37		18.5%
Dystocia (See Table XII)	23		62.1%

TABLE V. TYPES OF PELVES ENCOUNTERED AND PERCENTAGE OF DELIVERIES WITHOUT
AND WITH DYSTOCIA

	NUMBER	PER CENT
Gynecoid	80	100.00
No dystocia	47	58.75
Dystocia	33	41.25
Anthropoid	49	100.00
No dystocia	28	57.14
Dystocia	21	42.85
Android	47	100.00
No dystocia	21	44.68
Dystocia	26	55.31
Platypelloid	24	100.00
No dystocia	12	50.00
Dystocia	12	50.00
Dystocia in entire series	92	46.00

Prolonged Labor

In the entire series there were 17 patients, 8.5 per cent, in whom labor was classified as prolonged (Table VI). Of these, the shortest labor was 24 hours; the longest 48 hours; and the average 33.5 hours. The prediction of prolonged labor was made in only one instance by the dystocia clinic, and in the x-ray department only twice. Table VI shows that there was prolonged labor in 9 patients with contracted pelves, and in 8 with normal pelves. While this series is small, it at least points to the fact that there are other factors beside contracted pelvis involved in the prolongation of labor. In only 3 cases were excessive-sized infants found; and there was one fetal death.

Cesarean Section

Thirty-two cesarean sections were performed in this series, an incidence of 16 per cent. Table VII shows the clinic incidence of cesarean section for the year 1948-1949 to be 2.94 per cent. The high incidence of cesarean section in this series was not unexpected since these were segregated cases in which the incidence of abnormality was high, and a large number of patients who had had previous cesarean sections appear in this series. Maternal morbidity

occurred in 7 cases, an incidence of 21.8 per cent. Two patients had post-operative pneumonia, and 5 had puerperal endometritis. There was no fetal mortality in this group.

TABLE VI. ANALYSIS OF PROLONGED LABOR

Prolonged labor		17	8.5%
Prolonged labor in contracted pelves	9	
Forceps	7	
Cesarean section	2	
Prolonged labor in normal pelves	8	
Forceps	6	
Cesarean section	1	
Breech extraction	1	
Fetal mortality	1	
Stillbirth-shoulder dystocia		
Fetal weights		
2,500-3,000 grams	3	
3,000-3,500 grams	7	
3,500-4,000 grams	4	
4,000 grams and over	3	

TABLE VII. ANALYSIS OF CESAREAN SECTIONS

	NUMBER	PER CENT
Cesarean sections	32	16.00
Clinic incidence 1948-49	92	2.94
Indications		
1. Previous section with contracted pelvis (no labor)	13	
Contracted inlet only	7	
Contracted inlet and midplane	5	
Contracted midplane only	1	
2. Indicated after trial labor	11	
Contracted inlet only	9	
Contracted inlet and midplane	1	
Contracted midplane only	1	
3. Indication other than fetopelvic relationship	3	
Premature separation of placenta	1	
Pre-eclampsia, fulminating	1	
Uterine inertia, primary	1	
4. Previous section only	1	
5. Elective, para 0000, breech, contracted inlet	1	
6. Elective, elderly primigravida, contracted inlet	1	
7. Elective, previous stillbirth, contracted inlet	1	
8. Elective, para 0000, markedly contracted pelvis	1	
Types		
Laparotrachelotomy	25	
Extraperitoneal	7	
Maternal morbidity	7	
Fetal mortality	0	

Previous Section

Sixteen patients who had had one or more previous sections were encountered in our group, an incidence of 8 per cent (Table VIII). In our clinic routine placentography is performed in all patients who have had a previous section. In this series 5 placentas were found by x-ray to be located beneath the previous operative site. In such instances it is our usual practice to perform an elective repeat section—not so much because we fear an increased incidence of rupture of the uterus, but because, if rupture should

occur, it would be infinitely more formidable to both mother and baby. It will be noted that only two patients were delivered vaginally who had had previous sections.

TABLE VIII. PREVIOUS CESAREAN SECTIONS SHOWING METHOD OF DELIVERY OF PRESENT
                                   PREGNANCY

		NUMBER	PER CENT
Previous cesarean sections		16	8.0
Pelvic delivery, term baby		2	
Contracted pelvis	2		
Abdominal delivery		14	
Previous section and contracted pelv.	13		
Previous section only	1		
Types of section, laparotrachelotomy		14	
Maternal morbidity		2	
Puerperal endometritis	2		
Placentography showed placenta under scar in		5	

Premature Delivery

From Table IX we observe that there were 13 premature deliveries, or 6.5 per cent for the series. Twelve patients were delivered vaginally, and one abdominally. All premature babies survived. The clinical concept that premature labor occurs more frequently in patients with contracted pelves was not borne out by our study since the clinic incidence of all premature livebirths in the year 1948-1949 was 6.8 per cent, while the incidence of premature delivery in the contracted pelvis group in this series was 4.32 per cent.

TABLE IX. PREMATURE DELIVERY

Premature delivery		13	6.50%
Contracted pelvis	7		4.32%
Normal pelvis	6		
Vaginal delivery		12	
Abdominal delivery		1	
Fetal mortality		0	

Excessive-Sized Infants

Table X shows that there were 5 infants weighing over 4,000 grams. The one stillbirth in this group was due to shoulder dystocia.

TABLE X. INFANTS WEIGHING OVER 4,000 GRAMS

Excessive-sized infant		5	2.50%
Vaginal delivery	4		
Abdominal delivery	1		
Contracted pelvis	3		
Normal pelvis	2		
Stillbirth (shoulder dystocia)	1		

Presentation and Position

A total of 27 abnormal presentations and positions, or 13.5 per cent, occurred in this series, the data being presented in Table XI. In the entire series 17 occiput posterior positions (8.5 per cent) were encountered. Of a total of 49 anthropoid pelves in the series, 8 were associated with occiput pos-

terior position, and all of these patients were delivered vaginally. In 9 patients, or 4.5 per cent, breech presentation occurred. Three were delivered abdominally, 2 because of previous section with contracted pelvis, and the third because of a very small android pelvis in a primigravida. Pelvic delivery in breech presentation was undertaken when the fetus was estimated to be small and pelvic studies failed to reveal major pelvic contraction. There was one premature breech delivery and there was no fetal mortality. There was only one transverse lie which occurred in a patient with a small android pelvis.

TABLE XI. PRESENTATION AND POSITION

		NUMBER	PER CENT
Occiput posterior position		17	8.5
Anthropoid pelves associated		8	
Pelvic delivery		14	
Indicated operative delivery		14	
Abdominal delivery		3	
Breech presentation		9	4.5
Normal pelvis		6	
Pelvic delivery		6	
Full term	5		
Premature	1		
Contracted pelvis		3	
Abdominal delivery		3	
Average fetal weight:	2,833 grams		
Transverse presentation		1	0.5
Abdominal delivery		1	

Midplane Contraction

Table XII presents data concerning 37 patients, 18.5 per cent, who were found to have contracted midplanes either alone or in association with inlet contraction. Twenty-three, or 62.1 per cent, who had midplane contraction experienced dystocia. This incidence of dystocia would appear high in view of the over-all incidence in the series of 46 per cent. However, it is in line with Eller and Mengert's[6] observation that there is a high incidence of necessary operative delivery in midplane contraction. There was a fetal mortality of two in this group, one being a fetus which died in utero one week prior to the onset of labor, while the other was a neonatal death following forceps delivery. Autopsy in this case disclosed intracranial hemorrhage.

TABLE XII. MIDPLANE CONTRACTION IN WHITE AND NEGRO PATIENTS

		NUMBER	PER CENT
White	Total	4	2.0
No dystocia		1	
Dystocia		2	
Premature, pelvis not tested		1	
Fetal mortality		0	
Negro	Total	33	16.5
No dystocia		10	
Dystocia		21	
Premature, pelvis not tested		2	
Fetal mortality		2	
Prolonged labor		4	
	Total	37	18.5
Dystocia in entire series		92	46.0
Dystocia in midplane contraction		23	62.1

Comparison of Clinical and Radiologic Data

Table XIII represents the results of our clinical classification of pelves in the dystocia clinic on original pelvic estimation as compared with the radiologic classification. It will be observed that our predictions were correct in 125 cases, or 62.5 per cent; and that the pelvic type misdiagnosed most frequently clinically was the anthropoid type, a total of 31 such pelves being missed.

TABLE XIII. PELVIC TYPE FROM CLINICAL STUDY CHECKED AGAINST ROENTGEN STUDY

Correct		Total	125	62.5%
Gynecoid	68			
Android	25			
Anthropoid	18			
Platypelloid	14			
Incorrect		Total	75	37.5%
Gynecoid	13			
Android	21			
Anthropoid	31			
Platypelloid	10			

During our formative period in the dystocia clinic, which this survey covers, we attempted only to predict the outcome of labor as to pelvic or abdominal delivery. In the routine radiologic report, the X-ray Department also makes a prediction as to outcome. Table XIV shows a comparison of the results in this speculative field. In all fairness to the radiologists, it must be pointed out that we in the dystocia clinic had the decided advantage of our clinical examinations of the patient as well as our own study of the x-ray films to aid us in making our predictions. The value of trial labor in pelvic contraction is adequately demonstrated here when we consider that this was the course followed in the 17 cases which were delivered vaginally after the X-ray Department had suggested or stated as probable abdominal delivery. In a clinic where complete reliance is placed on x-ray pelvimetry, it is possible that 17 additional and unnecessary cesarean sections might have been performed.

TABLE XIV. PREDICTION OF TYPE OF DELIVERY BY DYSTOCIA CLINIC AND X-RAY DEPARTMENT

		NUMBER	PER CENT
Dystocia Clinic.—			
Correct		160	95.23
Incorrect		8	4.76
Pelvic predicted when abdominal necessary	8		
X-ray Department.—			
Correct		148	88.09
Incorrect		20	11.90
Abdominal delivery predicted when pelvic occurred	17		
Pelvic predicted when abdominal necessary	3		
Eliminated Group.—			
Elective cesarean section		6	
Section because of previous section		11	
Section for reason other than fetopelvic relationship		3	
Premature labor, pelvis not tested		11	
Baby, death of, in utero 1 week before labor		1	
		32	

Another factor which we checked in our clinical estimation against x-ray findings was the direction of the inclination of the side walls of the pelvis,

recording our impression as convergent, straight, or divergent. Our clinical impressions were correct in 116 cases, or 58 per cent; and incorrect in 84, or 42 per cent.

TABLE XV.   SIXTY-FIVE CASES IN WHICH CLINICAL MEASUREMENT OF TRANSVERSE ISCHIAL DIAMETER OF PELVIC OUTLET WAS 8.5 TO 6.5 CM.

CLINICAL MEASUREMENT OF TRANSV. ISCHIAL DIAMETER OF OUTLET, CM.	8.5	8.5 TO 8.0	8.0 TO 7.5	7.5 TO 7.0	7.0 TO 6.5	TOTAL	PER CENT
Total cases	30	23	9	2	1	65	100
Midplane interspinous diameter 9.0 cm. or less	6	3	0	1	0	10	15.3
Mengert's midplane index 105 or less	11	6	0	1	1	19	29.2
Contracted inlet associated	11	9	3	1	0	24	36.9
Premature, pelvis not tested	4	0	1	0	0	5	
Elective section	4	3	0	0	0	7	
Remaining cases						53	100
Dystocia	9	9	0	1	0	19	35.8
No dystocia	13	11	8	1	1	34	64.1

We were interested to learn whether or not a small clinical measurement of the transverse ischial diameter of the pelvic outlet pointed to pelvic contraction in other planes of the pelvis. Table XV shows our data in 65 cases in which this clinical measurement ranged from 8.5 cm. to 6.5 cm. It will be observed that the midplane interspinous diameter was found to be 9.0 cm.
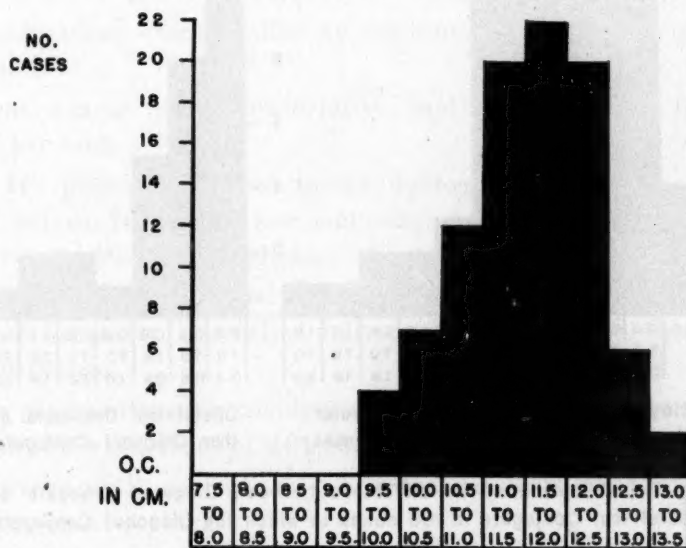
Fig. I Distribution of obstetrical conjugate (x-ray) in 92 cases in which diagonal conjugate was measured at 11.5 cm., or more. (after Dippel).

or less in only 10, or 15.3 per cent; and Mengert's midplane index of 105 or less was found in 19, or 29.2 per cent. It was noted that in 24, or 36.9 per cent, a contracted inlet was associated with a contracted outlet. Dystocia was encountered in 19, or 35.8 per cent. It may therefore be stated that our data show clinical contraction of the transverse ischial diameter of the pelvic outlet may point to contraction at the midplane in one out of every 3½ cases, and to contraction at the inlet in one out of every 3 cases.

Reference to Figs. 1 and 2 will show the relationship between the clinically measured diagonal conjugate and the obstetrical conjugate measured by x-ray. In 92 cases the diagonal conjugate was measured at 11.5 cm. or more, and the distribution of the obstetrical conjugate, measured by x-ray, is shown in Fig. 1. It will be seen that in only 4 cases did the obstetrical conjugate fall within the borderline area of contracted pelves (9.5 to 10.0 cm.). This confirms the work of both Jacobs[8] and Dippel.[9]

In Fig. 2 will be seen the distribution of the difference between the diagonal conjugate and the obstetrical conjugate in 108 cases in which the diagonal conjugate measured 11.5 cm., or less. The diagonal conjugate was equal to in 4 cases, and greater than the obstetrical conjugate in 72 cases. In the remaining 32 cases the diagonal conjugate was actually less than the obstetrical conjugate. We must therefore agree with both Jacobs[8] and Dippel[9] and conclude that in those patients in whom the diagonal conjugate is greater than 11.5 cm., an adequate pelvic inlet is to be anticipated; while in those in whom this measurement is less than 11.5 cm., x-ray pelvimetry is most certainly indicated.

Diagonal Conjugate equal to or greater than Obstetrical Conjugate. 76 cases.

Obstetrical Conjugate greater than Diagonal Conjugate. 32 cases.
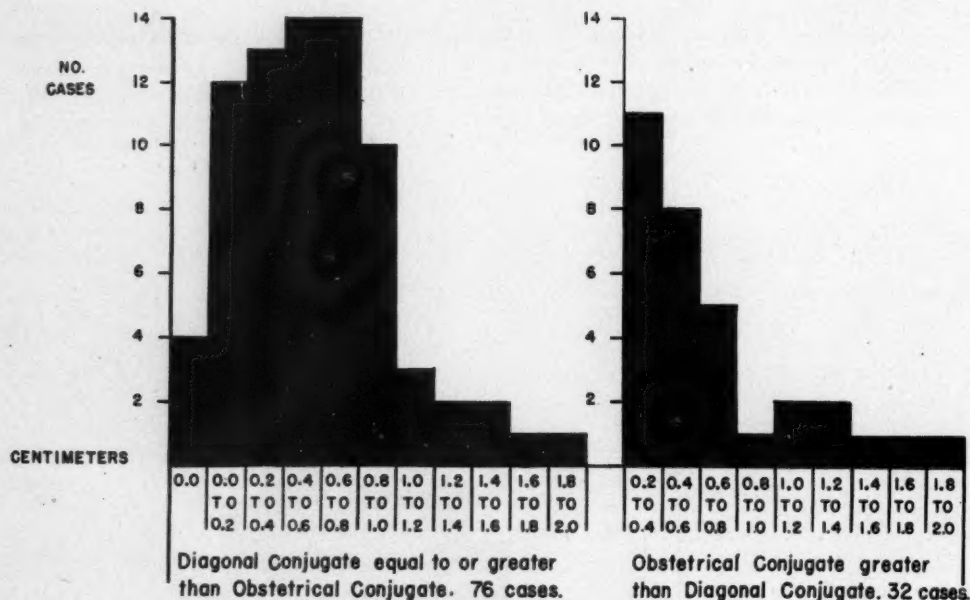
Fig. 2 Distribution of the difference between Diagonal Conjugate and Obstetrical Conjugate in 108 cases in which the Diagonal Conjugate was 11.5 cm., or less. (after Dippel).

We have attempted to demonstrate the significance and teaching value of the dystocia clinic in correlating clinical and roentgen pelvimetry. We would not wish to rely completely upon either of these methods because we believe that by a combined study we obtain an over-all impression of the architecture and capacity of the pelvis under consideration which would not be available from either method alone. While it is realized that the trained obstetrician can determine those cases in which x-ray pelvimetry should be done, certainly there are many individuals, devoting at least a part of their time to the

practice of obstetrics, who do not have this skill. Therefore, it is recommended that all of us teach that routine x-ray pelvimetry in the primigravida should be an essential part of prenatal care.

Since satisfactory methods of cephalometry and x-ray measurement of the transverse ischial diameter of the pelvic outlet are not available, these were not studied in our cases. Classical external measurements of the pelvic inlet are omitted in our clinic. This concept is in agreement with that of Eastman,[1] Greenhill,[10] and Titus.[11]

The maternal morbidity rate was 14.5 per cent, the major cause being 18 cases of puerperal endometritis. The chief maternal complication was complete perineal laceration in 14 cases. We have found Mengert's indices extremely useful as an aid in classifying pelves as contracted or not contracted. Trial labor is strongly advocated in all but grossly contracted pelves and when accompanied by vertex presentations. We believe that clinical and x-ray pelvimetry are not irreconcilable but complement each other and are of equal importance in the study of the obstetrical pelvis, and, combined, they give us invaluable assistance in the solution of clinical dystocia problems.

Summary and Conclusions

1. Two hundred cases studied by combined clinical and x-ray pelvimetry are presented.

2. There was no maternal mortality; and an uncorrected fetal mortality of 5, or 2.5 per cent.

3. Of 162 patients referred to the dystocia clinic because of suspected contracted pelves, 79, or 42.5 per cent, were found to have contracted pelves by application of Mengert's indices.

4. Anthropoid pelves barely outnumbered android in this series. The incidence of necessary operative delivery was highest in the android and platypelloid groups.

5. The cesarean section incidence was 16 per cent in this series as compared to the clinic incidence of 2.94 per cent.

6. Fourteen of 16 patients who had had previous cesarean sections were subjected to repeat section.

7. The incidence of prematurity in our series was not increased over the general clinic incidence.

8. A total of 27 abnormal presentations and positions, or 13.5 per cent, was encountered.

9. Of 37 patients who had midplane contraction, 23, or 62.1 per cent, had dystocia. The incidence of midplane contraction was 18.5 per cent.

10. From clinical pelvimetry the pelvic type was correctly predicted in 62.5 per cent; while the type of delivery (pelvic or abdominal) was correctly predicted in 95.23 per cent.

11. Trial labor is strongly advocated in all but grossly contracted pelves and when accompanied by vertex presentations.

12. In those cases in which the clinical measurement of the transverse ischial diameter of the outlet is 8.5 cm., or less, one may expect contraction of the midplane in one out of every 3½ cases, and contraction of the inlet in one out of every 3 cases.

13. Clinical measurement of the diagonal conjugate was found to be satisfactory in only those patients in whom this measurement was more than 11.5 cm. It is urged that all patients in whom this measurement is less than 11.5 cm. be given the benefit of roentgen pelvimetry.

14. A combined clinical and roentgen study of the obstetric pelvis is advocated.

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6 EAST READ STREET

Discussion

DR. PAUL TITUS, Pittsburgh, Pa.—The first point about Dr. Savage's paper to be commended is that there should be correlation between these two methods of pelvimetry. Neither method displaces the other; roentgen pelvimetry has added to the information to be gained from clinical pelvimetry so that accuracy of predictions regarding dystocia has been greatly increased by this correlation between methods.

Two findings in this study are especially worthy of comment. Dr. Savage reaffirms the belief that outlet contraction in the bisischial diameter (a clinical measurement) will be accompanied in at least one-third of all instances by significant midplane contraction (an x-ray finding of greatest importance).

He repeats the entirely correct contention that the finding of a diagonal conjugate of 11.5 cm. is a definite indication for x-ray. However, a longer diagonal conjugate does not make an x-ray unnecessary because serious dystocia can occur in an anthropoid type of pelvis.

I can make no more than a small contribution to this excellent paper. What I wish to offer is a copy of the x-ray obstetrical chart used in the St. Margaret Memorial Hospital in Pittsburgh. It combines the essential diameters taken by the Thoms technique with the area estimations of Mengert, combines the Caldwell-Moloy and the Thoms morphologic classifications, presents tables of normal diameters for reference, and in addition to the x-ray study has a space for the obstetrician's evaluation of the films and his prediction based on this correlated with his clinical findings.

ST. MARGARET MEMORIAL HOSPITAL

X-RAY REQUEST

CHECK
Walk
Chair
Stretcher

Name
Address
Part to be examined
Doctor making request
Brief clinical history of case

In-Patient
Out-Patient
Date

FOR DEPARTMENT OF OBSTETRICS

Special Notes

PELVIC MEASUREMENTS

	A.P.	Trans.	P. Sag.	Area A.P. x Tr.	(Area Norm.²)
Inlet	cm.	cm.	cm.		(145)
Midplane	cm.	cm.	cm.		(125)

1. Reduction to 85% of aver. plane capacity equals dystocia contraction; (123.25 inlet 106.25 midplane)
2. 180% inlet—75% midplane capacity worse than reverse relation.
3. Reduction both planes: more dystocia with relatively less reduction. (Mengert)

TYPE: Averages for	DOLICHOPELLIC (ANTHROPOID) ☐	MESATIPELLIC (GYNECOID) ☐	BRACHYPELLIC (ANDROID) ☐	PLATYPELLIC (PLATYPELLOID) ☐
Inlet				
Anteroposterior	12.0 —13.0	11.5 —12.25	10.5 —11.5	
Transverse	11.5 —12.25	12.0 —12.75	12.25 —13.25	
Posterior Sagittal	4.5 — 5.5	4.25— 5.0	4.5 — 4.5	
Midplane				
Anteroposterior	12.0 —13.0	11.75—12.0	11.5 —12.75	
Transverse	9.25—10.25	10.0 —10.75	10.0 —11.0	
Posterior Sagittal	4.75— 5.5	4.5 — 5.5	4.5 — 5.5	

CONTOUR DESCRIPTION

Pelvic Inlet:	Symmetrical	Asymmetrical	
Inlet Forepart	Wide	Average	Narrow
Sacrosciatic Notch:	Wide	Average	Narrow
Sacral Curve (lateral):	Angulated	Average	Straightened

FETUS:	Single	Multiple	
Presentation	Vertex	Breech	Other
Relation to Inlet	Above	Dipping	Engaged

PLACENTA:
Location of

Signed   M.D. Roentgenologist

REVIEW—PROGNOSIS:

Note: Two (2) copies required; one (1) for Dept. of Obstetrics, one (1) for attending obstetrician.

Date   19   Signed   M.D. Obstetrician

DR. J. BAY JACOBS, Washington, D. C.—I am in accord with the views presented by the essayist. I believe that all obstetricians should evaluate pelves as described. I have been following this procedure since 1928, both in private and clinic practice. I like the method by which Dr. Savage selects his cases for the dystocia clinic—those patients who have had previous cesarean section, history of previous dystocia, unexplained still-birth, prolonged labor, or who actually appear to have a contracted or borderline pelvis; that just about covers the field.

It is surprising that there is any question about the evaluation of external measurements and x-ray pelvimetry. They both have definite value.

I am opposed to discarding external measurements, from the teaching point of view. We know that where the external conjugate is diminished markedly in size, one might expect difficulty. That of course, depends upon the type of individual; for instance, such factors as the amount of adiposity, the thickness of skeletal bones and the general struc-

ture of the person should be taken into consideration, in evaluating the significance of Baudelocque's diameter. The external transverse diameters of the inlet, namely the interspinous and intercristal, do not have great significance since they are affected by the amount of flare of the iliac bones. Clinically, configuration of the pubic arch and the transverse diameter of the outlet are important and cannot be estimated as accurately by x-ray.

Roentgen pelvimetry does have many advantages. On the lateral film, one can determine the true conjugate accurately, as well as the anteroposterior diameter of the midpelvis and the posterior sagittal. The anteroposterior film enables accurate determination of the transverse diameter of the inlet.

Of course, we prefer to be confronted with inlet rather than midpelvic or outlet contraction since in the latter two we assume more risk and have to depend upon previous experience in estimating possibility of delivery through the pelvis.

The author states that he has very little confidence, or at least gives me that impression, in cephalic measurements and the estimation of outlet contraction by x-ray. I have already referred to the value of roentgenography in measuring the outlet. I have confidence in cephalometry to the extent that in the lateral film when taken in the standing posture one can obtain, in most instances, the size of the biparietal diameter, and can estimate with reliability the degree of maturity of the fetus, as well as other important incidental factors such as degree of descent and amount of flexion.

Again I wish to stress the fact that one should not be misled by estimated measurements of the true conjugate diameter. It is better to place confidence in the length of the diagonal conjugate, which can be measured reliably by Smellie's technique. As an example, I might mention two patients in whom the diagonal conjugates were equal but the true conjugate in one actually measured 10.2 cm. and in the other 12.3 cm., a difference of 2.1 cm. This was due to the fact that in the latter patient the angle between the symphysis and diagonal conjugate was 24 degrees greater than in the former. The desirability of resorting to x-ray pelvimetry where the diagonal conjugate is 11.5 cm. or less in a primipara and 11 cm. or less in a multipara, is evident.

Relative to the statistical reports of the essayist, I would like to say that 14 complete lacerations is considered rather high, in my opinion. We realize that these deliveries were performed by residents and I believe it would be well to instruct them to perform mediolateral episiotomies in cases of borderline outlet. In such cases also, spontaneous delivery should be favored if possible, rather than forceps delivery, for less trauma would be incurred by the mother and baby.

In conclusion I may state that I am in hearty accord with the method of study, that the results were good and that the incidence of cesarean section, omitting patients in whom the operation was performed because of previous cesarean section, was only 8 per cent. In my paper, dealing with a large series of patients with borderline pelves, presented before this Association several years ago, there was a 6.2 per cent incidence of cesarean section. It is my opinion that the author's clinic is conducted in a conservative and intelligent manner.

DR. T. L. MONTGOMERY, Philadelphia, Pa.—I have been particularly interested in this paper because it presents the organization of a clinic for the study of disproportion in a teaching institution and illustrates especially well how such a clinic can be correlated in the educational program. That, I feel, is an exceedingly important consideration, especially that these cases should not be withdrawn from the general clinic where students have contact with them and have an opportunity to study this problem with competent instructors. The problem of whether x-ray pelvimetry shall or shall not be taught is rather an academic subject. I think all of us realize that x-ray pelvimetry is a relatively small part. I sometimes wonder whether if the x-ray techniques are routinely employed the resident or the intern would really study the pelvis and study the anatomic configuration and the relation as if external pelvimetry were not practiced. Routine x-ray of our primigravida patients is at least a medium of insisting upon the general relationship.

And again, from the academic standpoint, I think much can be said for it, but I am not sure yet, and I am not sure that anyone is certain, that x-ray is entirely unharmful, particularly where x-ray may have to be repeated later. There have been so many instances where we have had to change our mind at a later date, realizing that what we have been doing has been detrimental. I would like to hold off on the x-ray until we have clinical evidence of disproportion. I would rather hold fire until the patient is in labor. Granted that these studies should be made often, it is most helpful to repeat the x-ray during labor and often the information with regard to the fetal head or fetal parts, and particularly after rupture of the membranes, is the important consideration in the final decision as to what should be done.

DR. E. L. KING, New Orleans, La.—I feel that we should by all means teach and practice clinical pelvimetry. In doubtful cases I believe that we should do both clinical and x-ray studies. In many primigravidas, granted the fetus is not too large, we can determine whether it can come through by clinical methods alone. If in doubt we fall back on the x-ray; also in multigravidas who have had trouble or in whom there is evidence of a small pelvis. The Mengert index is good but it must be correlated with the size of the baby. The roentgenologists who do our work give us very good estimates of the size of the fetal head. We have checked this many times immediately after delivery, especially after cesarean section, when the head has not been molded, and we find very close correlation.

DR. SAVAGE (Closing).—In regard to Dr. Jacobs' point concerning exact cephalometry, we have not had the good fortune he has had in his clinic to correlate exactly the actual measurements of the diameters of the fetal skull with those obtained roentgenographically. We do agree with him that the degree of maturity of the fetus and many other valuable considerations regarding cephalometry may be obtained from the films. We also agree that the films taken during labor are very valuable. Many of the cases we presented had lateral films taken during labor. We agree that 14 complete lacerations of the perineum are not to be desired. These patients were all delivered over midline episiotomies, which are routine in our clinic, and I think that probably explains the high incidence in this group.

In reference to Dr. Montgomery's remarks concerning the routine x-ray, you see from our presentation we are not doing it but simply advocating it so that we were speaking of the ideal in clinics such as that of Thoms, where all patients have routine roentgen pelvimetry. We agree with Dr. Montgomery that x-ray is valuable, and further agree with Dr. King that clinical and x-ray studies of the pelvis should go hand in hand. We do not wish to displace one with the other. We also agree with Dr. King that we must correlate the architecture as well as the indices of the various planes with the size of the baby, the presentation, the forces of labor, and all other factors which enter into the management of dystocia.

RUPTURE OF THE UTERUS*

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PERUSAL of 727 articles confirms the opinion that rupture of the pregnant uterus is a very serious accident and emphasizes the fact that although much has been accomplished in prevention and treatment of ruptured uteri the ultimate goal has as yet not been attained.

Classification

We prefer to divide all cases of uterine rupture into two major groups: viz., cesarean and noncesarean. In each category spontaneous is employed to indicate self-engendered ruptures which occur without intervention, while induced is used to include ruptures resultant from applied exogenous force. The latter term is considered preferable to "traumatic" inasmuch as all uterine ruptures are injuries. The chief causes are versions and extractions, forceps, oxytocics, and other means employed to hasten delivery. It has been customary to classify uterine ruptures further into complete and incomplete varieties depending upon the continuity of the peritoneum; however, a statement as to the location and extent of the rupture in each case is much more informative. An incomplete rupture resulting in profuse hemorrhage into the broad ligament is much more serious than a small complete one which is causing little or no bleeding.

Incidence

In evaluating statistics one must be mindful that hospital figures are largely influenced by complicated and mismanaged cases which gravitate to institutional practice; the reported incidence of ruptured uteri occurring at home is unreliable inasmuch as some of the cases are not recognized, purposefully or otherwise; and, in the *International List of Causes of Death*, uterine rupture is included without segregation with a number of other conditions. Dublin[1] reports that there were 4,122 maternal deaths in the United States in 1948. Applying Eastman's[2] statement that rupture of the uterus is responsible for at least 5 per cent of all maternal deaths, one concludes that over 200 women in this country thereby lost their lives that year. Table I shows the incidence in series reported from several United States hospitals during the past 25 years. Space limitations made it necessary to accept 20 cases as a minimum. Whitacre and Fang[13] reported 44 ruptures managed at a hospital in China, finding an incidence of 1:95. Frid[14] found 31 case records at a Buenos Aires institution (1:1,005). Davis and Gready[15] stated that there were 30 ruptured uteri at Chicago Lying-in Hospital, 1931-45 (1:1,600). In 1944 Cosgrove[16] mentioned 32 ruptures at Margaret Hague Maternity Hospital

(1:2,094). Burkons,[17] in a discussion of 45 ruptures occurring in 41 Ohio hospitals, stated that 12 occurred at St. Luke's Hospital in Cleveland (1:1,485). Tollefson[18] in 1944 presented summaries of 14 cases and stated, "During the past ten years at the Los Angeles County General Hospital 25 cases have been recorded, an incidence of 1 in 1,370 deliveries." Table II reveals the incidence trend in our institution. As pointed out in a previous communication[19] more normal cases have been admitted for delivery as time has elapsed. Ninety-six cases of ruptured uteri were managed at the Charity Hospital of Louisiana at New Orleans from Jan. 1, 1913, to July 1, 1950, during which time there were 127,522 deliveries (1:1,328). During the past twelve and one-half years the incidence has been approximately 1:1,800.

TABLE I. REPORTED INCIDENCE

HOSPITAL	PERIOD	AUTHORS	RUPTURES	DELIVERIES	RATIO
N. Y. Lying-In	1909-26	Davis	106	91,208	1:860
31 Phila. County	1931-41	Dugger	105	318,103	1:3,029
New Orleans Charity	1913-50	Present Study	96	127,522	1:1,328
5 New York	1932-46	Brierton	57	111,753	1:1,961
Johns Hopkins	1900-45	Delfs and Eastman	53	53,574	1:1,010
U. of Md. & Balt. City	1920-43	Morrison and Douglass	45	65,916	1:1,465
Boston City	1920-45	Lynch	44	41,706	1:1,118
Cook County	1928-48	Fitzgerald, Webster and Fields	42	92,226	1:2,196
Los Angeles County	1923-34	McNeile and McBurney	30	17,350	1:578
Boston Lying-in	1918-34	Sheldon	26	47,554	1:1,829
U. Hos. Cleve. & O.P.D. West Res.	1925-41	Bill, Barney, and Melody	23	63,391	1:2,756

TABLE II. INCIDENCE AT NEW ORLEANS CHARITY HOSPITAI

	RUPTURED UTERI	DELIVERIES	RATIO
1913-1925	23	10,752	1:467
1926-1937	26	33,245	1:1,278
1938-1950	47	83,525	1:1,776
	96	127,522	1:1,328

Age

In this series there is a predominance in the 26- to 30-year age group (Fig. 1). The youngest and oldest patients were both white, being 14 and 42 years of age. Reese and Linn[20] reported on a patient who was 48.

Gravidity and Parity

Trask[21] (1848) found 31 primigravidas in a collected series of 417 cases of ruptured uteri. Of his 75 cases Lobenstine[22] (1909) stated that 23, including 18 "incomplete ruptures" were in primiparas. In the subsequent New York Lying-In series of 106 cases, Davis[3] reported only 8 primiparas. Sheldon[11] found 2 primiparas in the Boston Lying-in group of 25 cases. Mahfouz[23] calculated a ratio of 15 multiparas to 1 primipara in 110 cases in Egypt. McNeile and McBurney[10] listed 1 primigravida in 13 patients who suffered uterine ruptures at the Los Angeles County Hospital. Four of the 42 patients reported on by Fitzgerald and associates[9] were nulliparas. Evaluating 53 ruptures, Delfs and Eastman[6] stated, "Not a single primigravida suffered spontaneous rupture of the uterus, despite the circumstance that the soft parts in these patients offer much greater resistance to the uterine forces than with higher parity brackets. Beyond question, increasing parity and age bring with them

certain changes in the uterine musculature which predispose to uterine disruption and, in our opinion, constitute the most important cause of spontaneous, noncesarean rupture.'' Figs. 2 and 3 depict the gravidity and parity of the Charity Hospital cases. Two of the 38 white patients were primigravidas. Five of the 58 Negro patients were nulliparas, including 3 primigravidas. One was a secundigravida and suffered a spontaneous rupture. There were 7 white and 10 Negro primiparas, of whom 3 had spontaneous ruptures. Eleven Negro and 5 white patients were parous for more than 6 times.
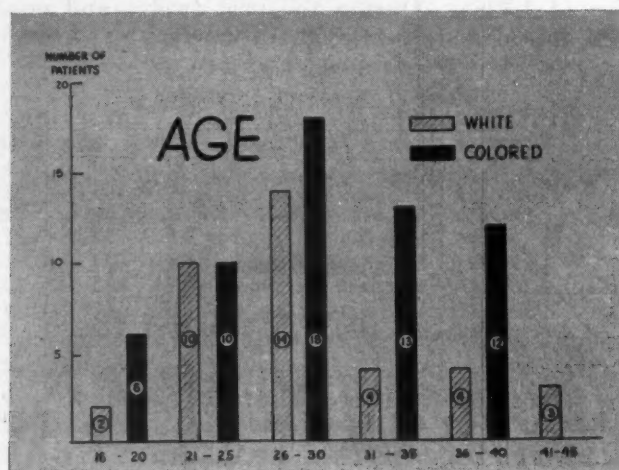
Fig. 1.

Onset of Rupture

Seventeen of the 23 cesarean and 67 of the noncesarean cases were in labor at the time of rupture (Table III). Although 16 of the cesarean cases were beyond the thirty-sixth week of pregnancy, 3 were in the 31- to 35-week group and 4 were in the 26- to 30-week stage. These data indicate that if all sectioned cases were scheduled for repeat sections 2 weeks prior to the expected date of delivery there would still be patients who would suffer spontaneous ruptures. Obviously, the element of unexpectedness may play a rather important role in cases of spontaneous rupture occurring before the onset of labor, especially in the noncesarean group.

TABLE III. ONSET OF RUPTURES

	CESAREAN RUPTURES		NONCESAREAN RUPTURES	
	SPONTANEOUS	INDUCED	SPONTANEOUS	INDUCED
Cases	22	1	29	44
Time.—				
During labor	16	1	25	42
Not in labor	6	0	4	2
Stage of pregnancy: weeks.—				
36-40	15	1	27	40
31-35	3	0	1	1
26-30	4	0	0	1
21-25	0	0	0	1
16-20	0	0	1	1

Location of Rupture

As tabulated (Table IV) the cervix was involved in 8 cases. Three ruptures extended into the corpus, and 2 into the broad ligament. In 25 cases the records indicated the "lower segment" as being the site of rupture. In 24 other cases the rupture was described and in 13 of these there was broad ligament extension. Three additional lower segment ruptures were at the site of section scars. In 2 cases the bladder was lacerated. Although there are a number of causes of gross hematuria during labor, its presence should always cause one to consider the possibility of uterine rupture. The corporal ruptures included 18 in scars and one at the site of a previous rupture. In 4 cases there was rupture of the fundus uteri.
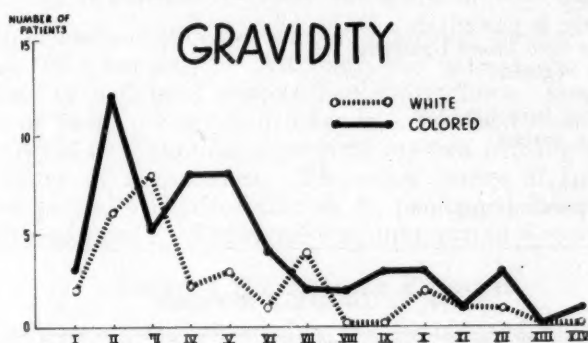
Fig. 2.
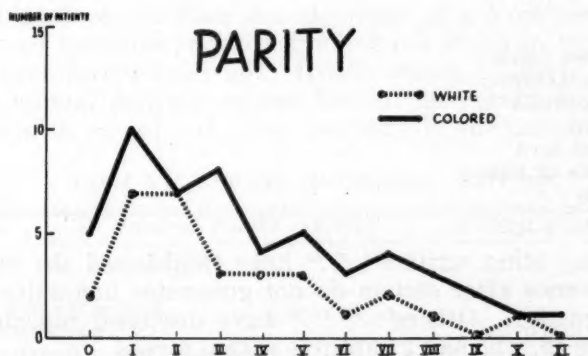
Fig. 3.

Cesarean Ruptures

As indicated by Table V, 23 patients had previously undergone cesarean section. Nineteen had had corporal incisions, 3 had been given the benefit of lower segment operations, and 1 patient (Case 53) had 1 corporal and 2 lower segment sections. She was operated upon at another institution in 1918, a corporal incision being made. A year later, a laparotrachelotomy was performed after "prolonged, hard labor." The following year a premature dead fetus was born. In 1924 she delivered "a normal 8-lb. baby after a very hard labor," being attended by a midwife. Three years subsequently another lower segment cesarean was done. In 1938 she returned with impending rupture. When the abdomen was opened, actual rupture in progress was observed in the

corpus uteri at the site of the first section.   Case 52 had a laparotrachelotomy in
1935 for "abruptio placentae."   Almost 2 years later she had a "normal de-
livery," and in 1938 the uterus ruptured spontaneously at term at the site of
the lower segment section.

TABLE IV.   LOCATION OF RUPTURE

Cervix into.—	
Lower segment	3
Lower segment & corpus	3
Lower segment & broad ligament	2
Lower Segment.—	
Anteriorly	8
Posteriorly	2
Anteriorly & posteriorly	1
Laterally into broad ligament	13
"Lower segment"	25
Section scar	3
Extending into bladder	2
Involving corpus	7
Corpus.—	
Section scar	18
Site of previous rupture	1
Fundus	4

TABLE V.   CESAREAN RUPTURES

23 Cases *6 Maternal Deaths (26.1%)* *15 Fetal Deaths (65.2%)*	
Type of Section.—	
Corporal	19
Lower segment	3
Both	1
Indication.—	
Contracted pelvis	1
Placenta abruptio	2
Placenta previa	7
Eclampsia	2
Prolapsed cord	1
Ankylosis of hips	1
Unknown	9

We[24] and many other writers[16, 25-34] have emphasized the fact that one or
more vaginal deliveries after section do not guarantee immunity to rupture in
a subsequent pregnancy.   Others[21, 30, 35-38] have discussed repeated rupture, as
exemplified by Case 15, who had 2 ruptures within a year.

Although Krukenberg[39] stated in 1886 that he believed that fully 50 per
cent of sectioned uteri ruptured during subsequent pregnancies, Sanger,[40] in
an 1895 report, presented a collected series of 500 cases without a single rup-
ture.   From 1895 to 1908, 20 cases of ruptured cesarean scars were collected
by Brodhead.[41]   In 1916, Findley[42] added 43 cases.   Bell[43] (1916) reported a
case and stated that he had found 5 additional instances.   In 1933, LaMariana[44]
reviewed the literature on rupture of the cesarean scar during pregnancy and
labor, finding 96 cases subsequent to Bell's[43] article and prior to 1933.   We have
been able to find a total of 459 cases of cesarean rupture reported in the litera-
ture since Jan. 1, 1908.

There has been a very considerable amount of investigation concerning
cesarean wound healing.   Mason and Williams[45] concluded that a firmly united
scar is stronger than uterine muscle.   Greenhill and Bloom[46] in a study of
uterine scars in 37 cases found healing by scar tissue in 31.   Schwarz and

Paddock[47] studied the histology of the section scar concluding that muscle regeneration plays a very minor part in the healing, and they consider fibroblastic proliferation as practically normal healing. As Lynch[8] states, "Although the uterine scar is satisfactory and competent, there is at present no means known of determining this very important fact, and even though sepsis and imperfect wound closure are causes of a faulty scar, it is also true that rupture can occur following an entirely normal convalescence and perfect surgical technique." Consequently, even if one knows why, where, by whom, how, and when the cesarean was performed, one still cannot vouch for the integrity of the scar even though the postoperative course was smooth.

Spontaneous Noncesarean Ruptures

This group consists of 29 cases with 13 maternal deaths (44.8 per cent) and 24 fetal deaths (82.8 per cent). Although one patient was a nullipara and 3 were primiparas, 15 had been parous 5 or more times. One of these patients had had 2 sets of twins. Four had toxemia. Two had malpresentations. One had placenta previa and another a cervical myoma causing dystocia. A third gave a past history of a curettage. The other causes of spontaneous rupture were contracted pelvis, 3; hydrocephalus, 2; prolonged labor, 2; and total placenta previa with accreta, 1. The cause was unknown in 6 cases.

Induced Noncesarean Ruptures

Table VI presents data concerning the 44 induced noncesarean ruptures. Versions and extractions were known to be responsible for 9 ruptures. The procedure following the administration of pituitary extract proved disastrous in an additional 2 cases, and in one it caused rupture when performed through an incompletely dilated cervix after the expulsion of a Voorhees bag. Obviously, all of the induced ruptures resulted from errors which in turn claimed a large maternal and even larger fetal toll. Lynch[8] states, "Rarely does a tear which accompanies a normal delivery extend beyond the cervix, but this unfortunate accident occurred in one of our cases, resulting in the patient's death."

TABLE VI. INDUCED NONCESAREAN RUPTURES

44 Cases	27 Maternal Deaths (62.8%)	35 Fetal Deaths (79.5%)	
	CAUSES		CASES
Forceps			9
Version and extraction			9
Breech extraction			4
Breech extraction and craniotomy			3
Pituitary extract			3
Pituitary extract, version and extraction			2
Forceps and craniotomy			2
Bag			2
Attempted version			2
Pituitary extract and attempted forceps			1
Manual dilatation of cervix			1
Bag, version and extraction			1
Pituitary extract with forceps and attempted craniotomy			1
Pitocin			1
Not stated			3

Mortality

All writers stress the high maternal and even higher fetal mortality following rupture of the uterus. Gordon and Rosenthal[48, 49] discussed "Diagnosis and Management of Rupture of the Uterus With a Study of 64 Maternal

Deaths'' occurring in a decade in Brooklyn. Twenty-seven ruptures were spontaneous and 37 were induced. They pointed out that rupture took place in the lower segment of the uterus in all but 3 cases and that cervical scarring is an important etiological factor. They concluded that internal version is the most frequent cause and should be recognized as an extremely hazardous procedure under certain unfavorable conditions and that strong fundal pressure can rupture a uterus as shown by 3 cases in their series. Four deaths occurred from the use of pituitary extract during the first stage of labor.

White[50] discussed 30 deaths due to uterine rupture in New Jersey. Chief causes were multiparity, prolonged labor and dystocia, and trauma at delivery, version and extraction being most conspicuous. In 1947 Taylor[51] presented a series of 33 maternal deaths attributed to rupture of the uterus in Pennsylvania, concluding that Pituitrin alone is responsible for many uterine ruptures.

TABLE VII. MORTALITY

	CESAREAN				NONCESAREAN					
	SPONTANEOUS		INDUCED		SPONTANEOUS		INDUCED		TOTAL	
Maternal	6	27.3%	0	0%	13	44.8%	27	62.8%	46	47.9%
Fetal	14	63.6%	1	100%	24	83.8%	35	79.5%	74	79.6%

	WHITE		NEGRO		INTRARACIAL WHITE	INTRARACIAL NEGRO
Maternal	17	17.7%	29	30.2%	43.6%	50.9%
Fetal	27	29. %	47	50.5%	71. %	85.5%

TABLE VIII. LOCATION OF FETUS AND PLACENTA AT TIME OF DIAGNOSIS

	CESAREAN	NONCESAREAN
Fetus and placenta delivered	0	34
Fetus delivered, placenta in uterus	0	2
Fetus and placenta in uterus	12	7
Fetal head and placenta in uterus, fetal body in abdomen	0	3
Fetus in abdomen, placenta in uterus	2	10
Fetus in uterus, placenta in abdomen	0	1
Fetal head in uterus, fetal body and placenta in abdomen	0	1
Fetus and placenta in abdomen	9	11
Not stated	0	4

Table VII shows the mortality figures for the 96 cases managed at Charity Hospital. One of the 23 cesarean ruptures was caused by Pituitrin, consequently, it is placed in the induced category. The mother survived but the infant died. In the remaining cesarean cases there were 6 maternal deaths and 14 fetal fatalities. In the 73 noncesarean cases, 29 ruptures were spontaneous, resulting in 13 maternal deaths and 24 fetal deaths. The 44 induced noncesarean ruptures caused 27 maternal deaths and 35 fetal deaths. The maternal and fetal mortality rates are lowest in the cesarean group as the result of earlier diagnosis and more prompt treatment. Furthermore, in some cases of rupture at the site of previous section, hemorrhage is less pronounced. We agree with Waters[52] that induced ruptures usually occur in patients who have been long in labor, with ruptured membranes, potentially or actually infected, and with a history of one or many attempts at delivery. Hemorrhage, trauma, and repeated anesthetization render many of them vulnerable to shock and sepsis. The fetal mortality in spontaneous noncesarean ruptures is higher than that in the induced noncesarean due to the fact that such a high percentage of the babies

are extruded into the abdomen. The intraracial mortality proved to be higher for the Negro patients, indicating the tendency for procrastination on their part. Since almost one-half of the Charity Hospital cases ended disastrously for the mother and over three-fourths proved to be fatal for the fetuses, it is in order to analyze the situation briefly.

Fetal Mortality.—Fig. 4 is calculated on the basis of 93 cases, inasmuch as the outcome of one white and 2 Negro babies was not recorded in the charts. Although they may have survived we did not deem it advisable to include them in the figures, consequently, the calculations are based upon 38 white and 55 Negro cases. There were 74 fetal deaths, 27 white infants, 29 per cent, and 47 Negro infants, 50.5 per cent, with a total fetal mortality of 79.6 per cent. The fetal mortality in white infants has decreased from 88.8 per cent to 56.3 per cent. From Jan. 1, 1913, through Dec. 31, 1937, the fetal mortality in Negro
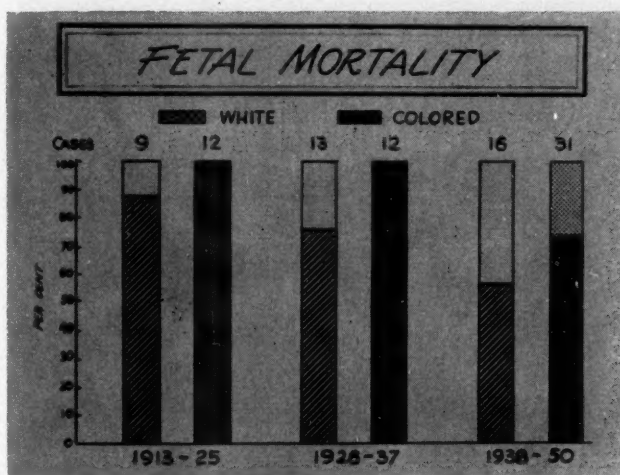
Fig. 4.

infants was 100 per cent. Since Jan. 1, 1938, it has been lowered to 74.2 per cent. A study of the fetal status at the time of the mothers' admittance to the hospital revealed that 43 fetuses were dead and 5 were nonviable. The latter are also included in the mortality tables inasmuch as rupture of the uterus was the cause of fetal death. Five babies had been delivered alive at home and 4 others were considered to be in poor condition at the time of the mothers' admittance. In 35 cases the fetal status was considered to be good. Table VIII is included because the location of the fetus and placenta at the time of diagnosis of rupture is obviously very important when one is analyzing fetal mortality figures.

Maternal Mortality.—A total of 46 (47.9 per cent) mothers lost their lives. Seventeen were white (17.7 per cent) and 29 were Negro (30.2 per cent). As revealed by Fig. 5 the mortality in the white patients has decreased from 60 per cent in the 1913-1925 period to 31.3 per cent in the 1938-1950 period. The figures for the Negro race in the same periods of time show a decrease from 76.9 per cent to 35.5 per cent. Fig. 6 depicts the maternal condition on hospital entry. Five of the patients were delivered at home by physicians with forceps, while 8 were known to have had attempted deliveries by midwives. The causes of maternal death are set forth by Fig. 7. The patient listed as having hemolytic anemia died as the result of a transfusion reaction.

Symptoms and Signs

So much has been written about symptoms and signs associated with rupture of the uterus a detailed discussion is not necessary. It should, however, again be emphasized that a marked variability may occur and each case must be individualized. One must take into consideration presence or absence of section scar; stage of gestation; duration of labor; site, extent, and cause of rupture; patient's condition, including complications; and fetal status, including abnormalities. One must also remember that sedation and/or anesthesia mask symptoms to the detriment of some patients. In the case of impending rupture there is usually abdominal and uterine tenderness. The elicitation of uterine scar tenderness is particularly important. There is usually failure to progress although uterine contractions are forceful. Furthermore, there is
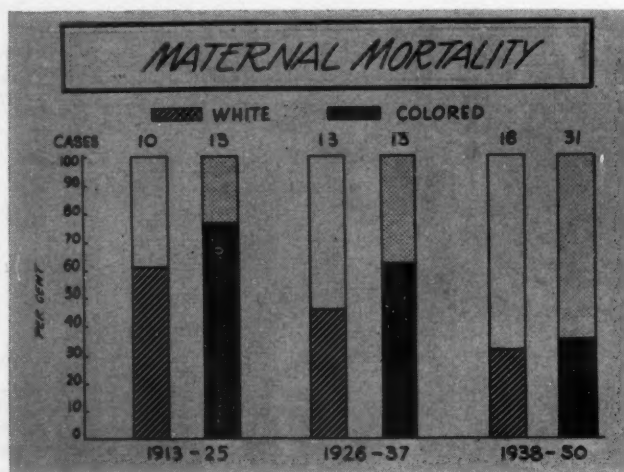
Fig. 5.

incomplete uterine relaxation in the interval between contractions. Tachycardia, restlessness, and exhaustion are usually present. Cooke[53] mentions the "intuition of the patient" and he also points out that chest pain of the diaphragmatic type may be associated with rupture of the uterus. Lynch[8] and others call attention to the fact that the round ligaments may be prominent and tense in association with a contraction ring. In cases of actual rupture of the spontaneous type, the patient characteristically experiences a severe tearing pain. In the conscious patient "labor pains" cease and the backache associated with labor disappears. In some instances, the patient passes through an interval in which she actually does not complain but on the contrary insists that she feels better. In certain cases the patient may be conscious of abnormally active fetal movements followed by fetal death. Examination reveals abdominal tenderness and by this time the patient may be having abdominal pain. There is recession of the presenting part if the fetus is extruded from the uterus into the abdomen. Hemorrhage, which may be of the internal, external, or combined type, usually occurs. If the patient has had a traumatic vaginal delivery the person in attendance may attribute the hemorrhage to cervical lacerations. Shock constitutes a very important role in the clinical picture of most cases. In days past, sepsis also played an important part.

Diagnosis

Any previous pregnancy difficulty which may have harmed the uterus should put one on guard. Certainly, if the patient has a history of having had difficult deliveries, she may have been the victim of uterine injury resulting in cicatrices which may give way during the stress and strain of the termination of the present pregnancy. She may have had an induced abortion with resultant uterine damage. Obviously, a history of cesarean section is very important. If the patient has had a hysterotomy the possibility of future pregnancy rupture must be borne in mind. Even though there have been relatively few cases of rupture of the uterus after myomectomy such a history must not be ignored. The history of cervical dilatation and uterine curettage is also to be remembered. All abnormalities of the present pregnancy, including those of labor, if this has started, must be properly evaluated. Surely, any patient
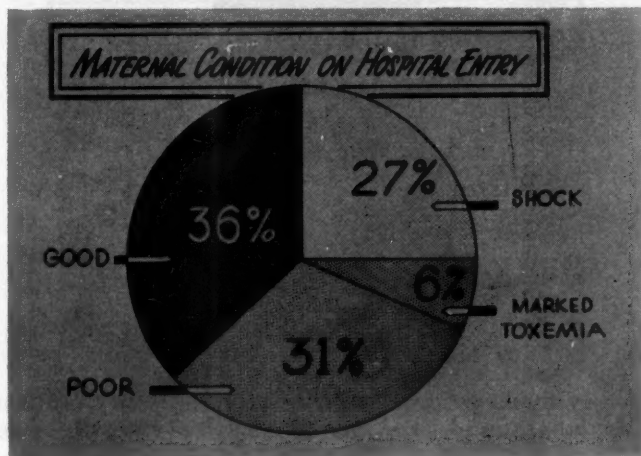
Fig. 6.

who exhibits mechanical dystocia should be considered as a candidate for uterine rupture. There may be abnormalities due to the mother's bony pelvis, the uterus, tumors in the pelvis, and abnormalities of the fetus, including hydrocephalus, monstrosities, abnormal presentations and positions, etc. The pain associated with some ruptures has already been mentioned. Hemorrhage and shock call for a prompt consideration of the possibility of uterine rupture until the contrary is proved. The cervix should be routinely examined after every delivery per vaginam. The uterine cavity should be explored and the lower uterine segment palpated after every difficult delivery. As in other fields of medicine the importance of actual examination of the patient cannot be overemphasized.

Treatment

Analysis of uterine rupture case records impresses one with the fact that the accident is usually preventable. Certainly, intelligent obstetric care would materially reduce the incidence of the condition and very greatly improve the maternal and fetal mortality. As Asa Davis[3] declared, "The time to treat rupture of the uterus is before it occurs. In the last analysis it means better, more conscientious and systematic care during pregnancy, labor, and the postpartum state." Obviously, in order to attain the ultimate, the cooperation of the patient is essential. We believe that every obstetric patient should be given the

benefit of blood grouping and Rh studies when first seen. Cases of previous
cesarean section must be managed with especial attention. The injudicious use
of oxytocics and manual or instrumental intervention of a questionable nature
in any case must be avoided. In the active therapy of rupture of the uterus,
blood transfusion and oxygen administration are indicated while preparations
are being made for immediate operation. Mengert,[54] Gustafson and Crump,[55]
and many others emphasize the importance of prompt treatment.
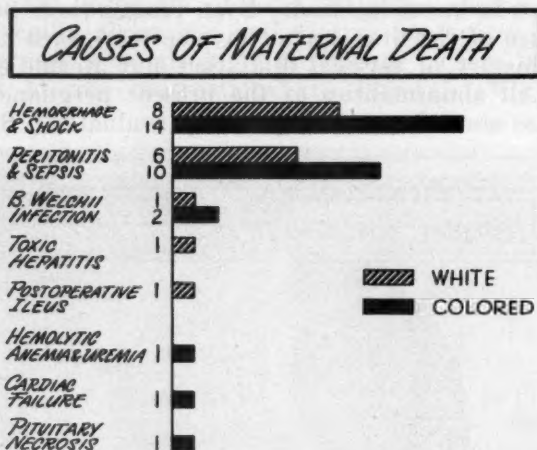
Fig. 7.

There is a very definite correlation between mortality and the time interval
from rupture to laparotomy. Of the 25 Charity Hospital cases subjected to
laparotomy within 2 hours, death occurred in only 2. It is generally conceded
that treatment should be hysterectomy as a rule. In certain instances, suture
of the uterus is technically easy and desirable because the patient strongly
wishes to have subsequent pregnancies or because of her age. Each case must
be individualized. Blood transfusions constitute an important part in the treat-
ment of rupture of the uterus. Fifty-three of the 96 patients received a grand
total of 77,100 c.c. of blood. The amount of blood and its rate of administration
should be determined in each case by the condition of the patient and the amount
of blood lost. Case 79 had a hysterectomy 30 minutes after rupture. She re-
ceived 1,000 c.c. of blood and progressed nicely. In emphasizing the great value
of massive transfusions, Lund and Brumfield[56] have reported Case 82, who re-
ceived a total of 7,500 c.c. of blood, hysterectomy being performed two and one-
half hours after rupture of a Couvelaire uterus. Case 73 is mentioned to serve
as a word of warning. The patient developed a severe reaction after receiving
200 c.c. of blood. Later she received 3,000 c.c. but died 4 days after operation,
the findings being compatible with transfusion reaction. In administering blood
one must exercise every precaution to prevent reactions and also to prevent
overloading the patient's circulation, as pointed out by Collins[57] and others.
Present-day available chemotherapeutics and antibiotics are wisely employed
to prevent and combat infection. Intestinal decompression is indicated in many
cases of uterine rupture and should be employed until peristalsis of the intestine
is satisfactory. Parenteral feeding, including the administration of dextrose,
vitamins, and electrolytes, is indicated. An indwelling urethral catheter is kept
in place to keep accurate check on the urinary output.

As shown by Fig. 5, there has been an improvement in the management of rupture of the uterus at Charity Hospital as the years have passed. Prior to institution of the residency system (July 1, 1937) the maternal mortality was 61 per cent. From Jan. 1, 1938, through Dec. 31, 1944, it was 55 per cent. Since the establishment of the blood bank it has been lowered to 12 per cent (Fig. 8). Consequently, the residency system, the blood bank, staff reorganization, and improved facilities have resulted in earlier diagnosis, adequate administration of blood, prompt operation, and the use of chemotherapeutics and antibiotics. From April 9, 1946, to Feb. 1, 1950, 20 cases of ruptured uteri were managed without the loss of a mother. Since then there has been one maternal death. When one considers fetal mortality figures one appreciates the fact that greater efforts must be exerted on the part of physicians and patients to prevent this very serious obstetric accident.
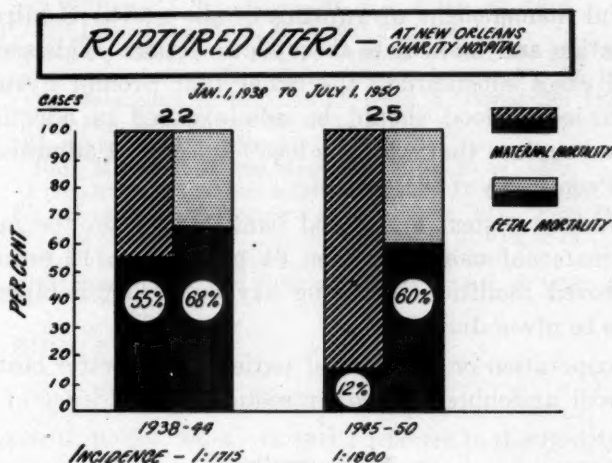
Fig. 8.

Summary and Conclusions

1. Ninety-six cases of rupture of the pregnant uterus have been managed at the New Orleans Charity Hospital from Jan. 1, 1913, to July 1, 1950, an incidence of 1:1,328 deliveries. Forty-seven cases occurred during the past twelve and one-half years (approximately 1:1,800).

2. A study of these records and a review of the available literature, in which we have been able to find data concerning a total of 1,728 cases (459 cesarean and 1,269 noncesarean) reported since Jan. 1, 1908, confirm the universally accepted opinion that uterine rupture is a very serious obstetric complication.

3. The high maternal (47.9 per cent) and even higher fetal mortality (79.6 per cent) in this and other large hospital series may be explained in part on the basis that complicated and mismanaged labors gravitate to institutional practice. Thirty-nine Charity Hospital cases were designated as emergencies at the time of admittance. Forty-three of the fetuses were dead and 5 were nonviable when the mothers arrived at the hospital.

4. Each obstetric patient should have information concerning her blood group and Rh status readily available at all times.

5. Every individual who has had a cesarean section is entitled to especially close supervision during each subsequent pregnancy in view of the fact that a patient who has had one or more vaginal deliveries after section is not necessarily immune to rupture of the uterus.

6. Any evidence of shock during pregnancy, the intrapartum state, or following labor should call for a prompt consideration of the possibility of uterine rupture. The cervix uteri should be examined immediately after each delivery and the lower uterine segment should be palpated after every difficult delivery or if there is any question as to extension of a cervical tear.

7. Successful management of rupture of the uterus requires alert evaluation of the situation and immediate therapeutic action. This series and a study of the reported cases substantiate the belief that prompt hysterectomy is the procedure of choice. Blood should be administered in adequate amounts to combat shock and replace that which is lost. Its rate of administration must be governed by the condition of the patient.

8. The residency system and blood bank have been the major factors in decreasing the maternal mortality from 61 per cent to 12 per cent in our institution. Improved facilities, including oxygen, chemotherapeutics, and antibiotics must also be given due credit.

9. Better cooperation on the part of patients plus better obstetric judgment and technique will undoubtedly further reduce the incidence of rupture of the uterus.

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Discussion

DR. F. J. LYNCH, Boston, Mass.—In 1944 I reported to this Society 44 ruptured uteri which had occurred at the Boston City Hospital in 25 years in 41,706 deliveries, which was an incidence of one in 1,118 patients. This is a greater occurrence than the one in 1,328 cases which Dr. Beacham reports from the Charity Hospital at New Orleans. Our maternal mortality was 52 per cent and the fetal mortality was 89 per cent. These figures are slightly higher than those reported by the essayist.

The number of cases that occur in a clinic is no gauge of the character of the work done, as many of the patients are sent in from the outside and their number will be influenced by the size of the area for which the emergency service is provided.

We agree with Dr. Beacham that the most important factor in the outcome for the mother is the promptness with which the diagnosis is made and with which appropriate treatment is instituted. The invaluable and irretrievable time that is frequently lost here, with the accompaniment of hemorrhage and shock and later sepsis, is the powerful element which results too frequently in a fatal termination.

In this series of cases, as in all others, the chief cause of ruptured uterus is forceps failure and version. The occasional predicament of the doctor those of us who do obstetrics can understand. A close decision is made to let the patient deliver from below and after permitting two hours of second-stage labor, a forceps delivery is attempted with failure. What to do? The bridges are burned behind us for a cesarean, the element of sepsis being too great. In desperation a version and extraction are attempted and it must be admitted are not infrequently successful, the worst happening frequently being the loss of the baby. But it is here that we have one of the greatest causes of ruptured uterus.

The successful termination of the delivery from below depends on the ability of the baby's head to configurate and mold, the vigor of the uterine contractions, and the char-

acter of the labor, all variable factors, and conditions impossible to foretell. The malleable head and a good labor result in success; and the hard, round, ossified head and a desultory labor spell failure.

It has always been an intriguing and fascinating speculation to me to explain why a head which has had the advantage of the molding, due to hours of labor, will refuse to advance with the powerful traction exerted with obstetrical forceps, and will come through the pelvis in many cases of version and extraction with the use of only moderate traction and the momentary application of the head to the pelvis.

My explanation of it is this: If the head is considered roughly of triangular shape with the base of it applied to the pelvic inlet, it is conceivable that it might be applied disadvantageously. When a version is done and extraction performed, the triangle is applied to the pelvic inlet by its apex and can be thus insinuated through the pelvis to its best advantage. The damage in these cases is done, of course, to the thinned-out lower uterine section in the process of the version.

To decide not to attempt the version and extraction, taking into consideration the number of times that one "gets away" with it, and to do a cesarean section, the safety of which has been tremendously compromised, is a difficult decision to make, and a maternal death with the late cesarean would probably receive much harsher criticism.

We constantly hear the admonition that too many cesarean sections are done. This is undoubtedly so, in cases in which the findings do not warrant subjecting the patient to the dangers of a section. But certainly in these cases under discussion too few elective sections are done, particularly in multiparas. The fact that a patient is a multipara and has had normal-sized babies through her pelvis is no guarantee that she may not have trouble in a present pregnancy due to a large baby, a postmature baby, or a hydrocephalus. In addition to the primipara at term with an unengaged head should be added the multipara with one hour of full dilatation with satisfactory labor and no progress, as a candidate for cesarean section. Again, loss of tone or senile changes taking place in the uterus, as pointed out by Eastman and emphasized by Dr. Beacham, place most of these cases in the upper age and parity brackets since these women are more susceptible to the possibility of a ruptured uterus.

Finally, one word in regard to treatment. Most statistics show that apparently the best results are obtained by means of a total hysterectomy as compared to those of supravaginal hysterectomy. While this is undoubtedly true on paper, I think these figures may be influenced by the fact that very likely only the more desperate cases are handled by the supravaginal method.

DR. LOUIS H. DOUGLASS, Baltimore, Md.—To implement what Dr. Beacham has already said, and to add one feature which has been omitted probably because of the time element, attention should be called to one type of rupture of the uterus which has not received quite as much attention as it deserves. In Maryland, in the two years, 1948-1949, there was a total of 95 maternal deaths. Ten, or a little over 10 per cent, occurred in women who had had their uteri packed for postpartum hemorrhage. All of them were multigravidas and most of them would fall in the classification of the "grand multipara." The deliveries had been normal and easy, the only complication of importance being the postpartum hemorrhage. Upon reviewing their histories a rather constant pattern was found; after the completion of the delivery, bleeding was severe and not controlled by ordinary methods and, in all, resort was had to packing. Since this did not control the bleeding, in some a second pack was introduced and in some the abdomen was opened after failure of one or two packs as the case might be. However, in all, this was done too late. Of the 10 patients, a definite diagnosis of rupture of the uterus was made, either at operation or at autopsy, in 3 there was a strong suspicion of rupture, but no operation or postmortem to prove it, and in only one instance could the condition be fairly definitely ruled out. The point which I would like to emphasize is that severe postpartum hemorrhage which does not respond to massage and the rather efficient oxy-

tocic agents, when given intravenously, particularly when it occurs in the multigravida, is quite likely to be due to a partial or a complete rupture of the uterus. If this be present, packing will not only do no good, but will actually be harmful in that vitally necessary time will be lost. In the 10 cases cited above, had this been kept in mind and a prompt laparotomy been done, it is more than probable that in our own State there would be 10 more mothers with their families today.

DR. BEACHAM (Closing).—The importance of early diagnosis and prompt treatment cannot be overemphasized. Blood replacement constitutes such a valuable part in the management of cases of rupture of the uterus, every obstetric service should have prompt access to an adequate blood bank. Furthermore, each obstetric patient should have information concerning her blood group and Rh status readily available at all times.

OXYGEN SATURATION OF THE BLOOD OF THE NEWBORN, AS AFFECTED BY MATERNAL ANESTHETIC AGENTS*†

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ANESTHETIC agents for parturition are chosen, to some extent, because of their minimal detriment to the infant. We have measured the effect of ether, nitrous oxide, Pentothal sodium, and cyclopropane on the oxygen saturation of the blood of the newborn infant during the early hours of life. The efficiency of supplementary neonatal oxygen has also been studied.

Eastman[1] has defined the normal oxygen content, capacity, and saturation of fetal cord blood. The average oxygen capacity of fetal cord blood at birth was about 21 volumes per cent. The blood from the umbilical vein at birth was found to be approximately 50 per cent oxygen saturated.

Smith[2] has shown that ether anesthesia does not materially reduce fetal oxygenation at birth, but that nitrous oxide and cyclopropane do reduce the amount of oxygen carried by the blood of the newborn at birth. Later, Smith and Kaplan[3] investigated the levels of blood oxygen saturation in normal infants during the first two weeks of life and determined the time necessary for the attainment of normal adult oxygen levels. In the usual case, one to three hours of extrauterine life find the newborn with oxygen saturation levels at or very near normal adult levels (91 to 98 per cent saturated).

This is a preliminary report dealing with the effects of anesthetic agents on oxygen saturation of the blood of the newborn. Elements that remain for further investigation are the effects of anesthesia on rates and depth of infant respiration; and the effect of anesthesia upon utilization of oxygen in the tissues. Then there are the problems of the effect of anesthesia upon hemoglobin, hydrogen ion concentration of the blood, and the carbon dioxide combining power of the blood.

Methods and Materials

The capillary blood oxygen capacities and contents were determined by the micromethod, described by Roughton and Scholander.[4] The heel of the newborn infant was cut, immersed in mineral oil, and blood was allowed to flow freely from the wound under oil; 0.5 c.c. of blood was gathered under oil in a heparinized syringe. Mercury was used as an agitator within the syringe. A total of 708 determinations were done upon 94 different infants.

Oxygen saturations in the neonatal period were studied from immediately after birth up until 18 hours of life, and the effects of various anesthetic agents were noted. All the infants were born vaginally by normal spontaneous or outlet forceps delivery. If respirations were not spontaneously established three minutes after birth, resuscitative measures were instituted.

All but 9 mothers received 100 mg. of Demerol and 0.5 mg. hyoscine from one to three hours before delivery. These 9 cases were scattered through the various anesthetic groups and showed no significant differences from the others in the same anesthetic group. The effect of supplemental oxygen was studied through capillary blood determinations done on newborn infants after the infants were placed in a Gordon-Armstrong incubator in which the atmosphere contained 50 to 60 per cent oxygen. The material studied and the anesthetic agents used are listed as follows:

ANESTHESIA	BLOOD SAMPLES	OXYGEN SUPPLEMENTAL	CASES
Pudendal or saddle block	Birth, 30 min., 1 hr., 3 hr.		20
Ether, 5 to 12 minutes	Birth, 30 min., 1 hr., 2 hr., 3 hr.		21
Nitrous oxide 80%, oxygen 20%, 5 to 7 minutes	Birth, 30 min., 1 hr.		10
Pentothal Sodium 2½%, 4 to 11 minutes	Birth, 30 min., 1 hr.		10
Oxygen 80%, cyclopropane 20%, 4 to 11 min.	Birth, 30 min., 1 hr., 3 hr., 12 hr., 18 hr.		13
Pudendal or saddle block	Birth, 30 min., 1 hr.	+	10
Ether, 5 to 12 min.	Birth, 30 min., 1 hr.	+	10
Total			94

Results

1. Twenty Full-Term Infants Whose Mothers Received Regional Anesthesia. The Infants Received No Supplementary Oxygen After Delivery. Determinations Done at Birth, One-Half Hour, One Hour, and Three Hourse (Table I).—
None of these infants required artificial resuscitation. It can be seen from Table I that there is wide variation in the oxygen content and percentage of saturation of the capillary blood. At the end of an hour of life 9 of the 20 infants had oxygen saturation values of 90 per cent or over. Ninety-one to 98 per cent oxygen saturation is considered normal for adults. The average oxygen saturation was 67.2 per cent at thirty minutes and 85 per cent at the end of the first hour of life. The average newborn infant's blood, one hour after delivery, is almost at normal adult levels if there has been no general anesthetic given to the mother during labor (Fig. 1).

2. Twenty-One Full-Term Infants Whose Mothers Received Ether Anesthesia Five to Twelve Minutes Before Delivery. The Infants Received No Supplementary Oxygen After Birth. Oxygen Determinations Were Taken at Birth, Thirty Minutes, Sixty Minutes, Two Hours, and Three Hours (Table II).—
The ether was given by open drop method for five to twelve minutes for the termination of the second stage of labor. The average oxygen saturation at the end of one hour was 79 per cent, and only 3 of 20 infants had values of 90 per cent or over. Eight of the 21 needed artificial resuscitation. Clinically, infants from this group did well, except for one who required 33 minutes of resuscitation.

Several capillary blood oxygen determinations were made at two and three hours after birth. At the end of two hours the oxygen saturation was
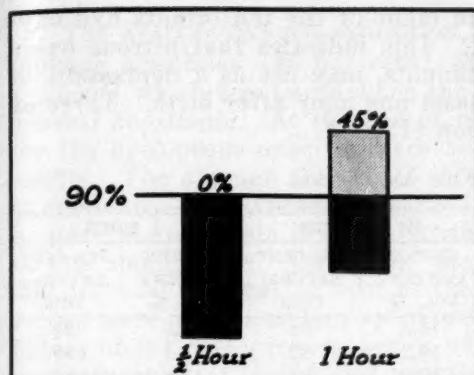
still depressed to an average value of 78 per cent. Even at the end of three hours, 6 out of eleven infants had oxygen saturation levels below 90 per cent. From this portion of the study we infer that three hours of life may not be sufficient for some newborn infants to recover fully from the effects of five to twelve minutes of maternal open-drop ether anesthesia (Fig. 2).

TABLE I. REGIONAL ANESTHESIA WITHOUT SUPPLEMENTARY NEONATAL OXYGEN

PA-TIENT	BIRTH			30 MINUTES		1 HOUR		3 HOURS	
	OXYGEN CAPACITY VOL. %	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION
1	18.8	8.7	46	13.4	71	13.7	73		
2	20.4	14.7	72	11.1	54	14.8	73		
3	18.9	10.0	53			17.3	92	15.9	84
4	19.0	5.0	26			15.7	83	18.2	96
5	19.1	7.0	37			18.3	96		
6	19.4	6.5	34			18.0	93		
7	17.4	13.8	79			15.3	88		
8	17.4	8.4	48	14.8	85	15.6	90		
9	16.0	8.7	54	10.6	66	13.1	82		
10	17.6	9.3	53	10.6	60	17.4	99		
11	20.9					20.5	98		
12	17.7					13.3	75		
13	16.9					11.6	69		
14	18.9					15.4	82		
15	17.6					12.3	70		
16	18.3					17.6	96		
17	16.1					13.9	86		
18	18.8					13.7	73		
19	19.1					17.2	90		
20	16.9					15.6	92		
Average	18.3	9.2	50.2	12.1	67.2	15.5	85.0	17.1	90

TABLE II. ETHER ANESTHESIA WITHOUT SUPPLEMENTARY NEONATAL OXYGEN

| PA-TIENT	BIRTH			30 MINUTES		1 HOUR		2 HOURS		3 HOURS	
	OXYGEN CAPACITY VOL. %	OXYGEN CONTENT VOL. %	PER CENT SATURATION	OXYGEN CONTENT VOL. %	PER CENT SATURATION	OXYGEN CONTENT VOL. %	PER CENT SATURATION	OXYGEN CONTENT VOL. %	PER CENT SATURATION	OXYGEN CONTENT VOL. %	PER CENT SATURATION
1	15.6	10.3	66	13.4	86	14.0	90				
2	16.1	9.9	62	7.3	45	14.2	88				
3	17.2	5.2	30	7.8	45	10.4	61				
4	18.6	10.4	56	14.8	80	15.9	86				
5	17.5	6.3	36	16.2	93	14.0	80				
6	15.4	6.3	41	7.7	50	10.2	66				
7	17.3	14.6	84	13.9	80	13.0	75				
8	17.2	12.1	70	10.9	63	11.8	69				
9	18.9	13.7	73	16.4	87	15.5	82				
10	20.3	12.9	64	14.6	72	16.2	80				
11	18.1					13.5	75	13.4	74	16.9	93
12	15.3					12.7	83	13.8	90	13.8	90
13	14.6					11.3	77	9.2	63	10.5	72
14	19.6					17.9	91	16.2	83	16.5	84
15	21.5					19.0	88	18.2	85	19.0	88
16	18.4							14.2	77	16.8	91
17	16.3					12.6	77	14.8	91	14.7	90
18	20.2					11.8	58	11.3	56	11.8	58
19	17.5					13.3	76	12.7	73	14.4	82
20	17.8	10.5	59			17.1	96			17.5	98
21	18.0	13.6	76			15.8	88	15.7	87	15.7	87
Average	17.7	10.5	59.7	12.3	70.1	14.0	79	14.0	78	15.2	85

REGIONAL ANESTHESIA

20 Infants—None Resuscitated

½ Hour Saturation— 67.2%

1 Hour Saturation— 85.0%

Fig. 1.- Percentage of Cases Above and Below 90 Per Cent Oxygen Saturation.
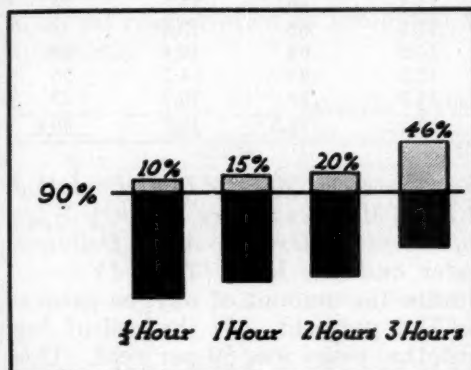
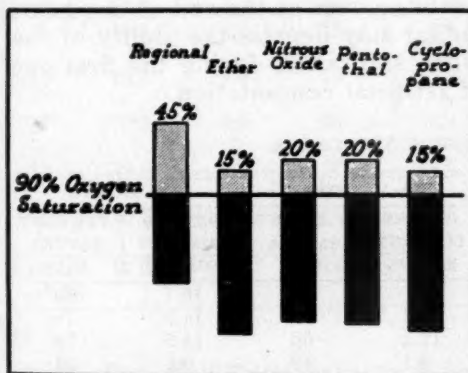## ETHER ANESTHESIA

20 Infants—8 Resuscitated

½ Hour Saturation— 70.1%
1 Hour Saturation— 79.0%
2 Hour Saturation— 78.0%
3 Hour Saturation— 85.0%

Fig. 2.- Percentage of Cases Above and Below 90 Per Cent Oxygen Saturation.

THE EFFECT OF MATERNAL ANESTHESIA ON THE OXYGEN SATURATION OF NEWBORN BLOOD AT THE END OF ONE HOUR.

Fig. 3.- Percentage of Cases Above 90 Per Cent Oxygen Saturation.

3. Ten Full-Term Infants Whose Mothers Received 80 Per Cent Nitrous Oxide Anesthesia and 20 Per Cent Oxygen, Five to Seven Minutes Before Delivery. The Infants Received No Supplementary Oxygen After Delivery. Determinations Done at Birth, Thirty Minutes, and at One Hour (Table III).—

The average oxygen saturation at birth was about 10 per cent below that experienced by infants born of mothers who received no general anesthetic agent but this difference was not statistically significant. Half an hour later the oxygen saturation averaged 74.5 per cent. At the end of an hour the

average saturation was 80.6 per cent, and eight of the ten infants had oxygen saturation values below 90 per cent. This indicates that nitrous oxide anesthesia, even when used in "safe" amounts, may act as a depressant to fetal oxygen levels in some cases for at least one hour after birth. Three of these infants required artificial resuscitation (Fig. 3).

TABLE III. NITROUS OXIDE ANESTHESIA

	BIRTH			30 MINUTES		1 HOUR	
PATIENT	OXYGEN CAPACITY VOL. %	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION
1	17.7	9.3	53	15.5	88	15.5	88
2	12.5	2.1	17	10.2	82	11.1	89
3	16.9	5.1	30	10.6	63	13.8	82
4	20.8	4.6	22	11.1	53	13.3	64
5	16.8	4.7	28	13.6	81	12.3	73
6	16.9	13.9	82	15.1	89	15.5	92
7	17.5	11.7	67	11.1	63	13.6	78
8	16.0	12.6	79	10.2	64	10.6	66
9	18.8	3.4	18	12.1	64	14.1	75
10	15.2	5.8	38	14.9	98	15.0	99
Average of 10	16.9	7.3	43.4	12.4	74.5	13.5	80.6

4. *Ten Full-Term Infants Whose Mothers Received 2½ Per Cent Pentothal Sodium Anesthesia Intravenously Four to Eleven Minutes Before Delivery Were Studied. These Infants Received No Supplementary Oxygen After Delivery. Determinations Done at Birth, Thirty Minutes, and One Hour (Table IV).—*

We note that at the end of thirty minutes the amount of oxygen saturation was relatively low. The average was 71.2 per cent. At the end of one hour the average oxygen saturation in Pentothal cases was 80 per cent. This is not significantly lower than that of infants born of mothers receiving no general anesthetic agents (Fig. 3), but in only 2 of the 10 Pentothal cases were the oxygen saturation values 90 per cent or over at the end of one hour. This part of the study suggests that Pentothal may depress the ability of the newborn infant to gain normal adult oxygen saturation during the first one hour of life. One of these infants required artificial resuscitation.

TABLE IV. PENTOTHAL SODIUM ANESTHESIA

	BIRTH			30 MINUTES		1 HOUR	
PATIENT	OXYGEN CAPACITY VOL. %	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION
1	17.7	11.9	67			16.7	94
2	19.2	10.0	52	14.1	73	14.9	78
3	18.6	10.5	57	12.2	66	14.5	78
4	18.7	8.3	44	9.1	49	9.5	51
5	17.9	6.9	39	12.3	69	14.5	81
6	21.2	14.9	70	13.9	66	16.2	86
7	18.6	5.6	30	13.2	71	16.2	87
8	20.3	9.0	44	15.8	78	16.7	82
9	18.6	10.5	57	15.8	85	17.0	91
10	18.6	8.0	43	15.6	84	15.2	82
Average of 10	19.0	9.6	50.3	13.6	71.2	15.1	80.0

5. *Thirteen Full-Term Infants Whose Mothers Received Four to Eleven Minutes of Cyclopropane Before Delivery. These Infants Received No Supplementary Oxygen After Delivery. Determinations Were Done at Birth, at Thirty Minutes, and at One Hour. Six Determinations at Three to Eighteen Hours (Table V).—*

The average oxygen saturation of the blood at birth with maternal cyclo-propane anesthesia (45 per cent) was not significantly less than that (50-55 per cent) which was found when the infants were born of mothers reeciving no general anesthetic. At the end of half an hour the oxygen saturation values for the cyclopropane series were below those found for the other anesthetic agents. The average for the 13 infants was 71.5 per cent oxygen saturation at one hour. The average is nearly 14 per cent lower than that measured when no general anesthesia is given but the difference is not statistically significant in this small series. Only 2 of the 13 infants had oxygen saturation levels that were 90 per cent or over at the end of the first hour of life. Since these values were still considerably depressed at the end of an hour, we studied 6 babies of the cyclopropane series with the idea of determining what the oxygen saturation of their blood was three to eighteen hours later. After twelve or more hours the neonatal oxygen saturation was at normal adult levels in but 2 of 5 cases. Seven of the 13 infants in the cyclopropane series required artificial resuscitation as compared with none in the group receiving regional anesthesia.

TABLE V. CYCLOPROPANE ANESTHESIA

	BIRTH			30 MINUTES		1 HOUR		NEXT SAMPLE	
PA-TIENT	OXYGEN CAPACITY VOL. %	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION
1	22.0	4.0	18			18.0	82	20.2 (3 hrs)	92
2	18.2	7.3	40	12.6	69	13.6	75		
3	20.7	8.3	40	13.0	63	12.7	61		
4	18.8	8.9	47	11.4	61	16.4	87		
5	19.0	12.3	65	17.5	92	17.0	90		
6	16.1	6.0	38	12.3	76	14.8	92		
7	12.0	3.4	28	7.3	61	7.8	65		
8	17.4	6.2	36	7.6	44	7.8	45		
9	18.6	2.2	12	1.8	10	7.6	41	14.5 (12 hrs)	78
10	19.2	14.9	78	12.2	64	12.9	67	15.4 (18 hrs)	80
11	19.2	9.5	50	8.4	44	12.8	67	16.9 (18 hrs)	88
12	18.3	6.7	37	10.6	58	12.9	71	17.4 (12 hrs)	95
13	15.5	13.9	90	11.3	73	13.3	86	15.1 (12 hrs)	97
Average of 13	17.9	8.0	44.5	10.5	59.6	12.9	71.5		88.3

6. Ten Full-Term Infants Whose Mothers Received Regional Anesthesia. Infants Were Placed in 60 Per Cent Oxygen Immediately After Delivery. Determinations Done at Birth, One-Half Hour, and One Hour (Table VI).—

There is considerable variation in percentage oxygen saturation of the fetal blood at birth. The average for the 10 cases was 55.4 per cent. By the end of 30 minutes, the 10 infants averaged 78.6 per cent oxygen saturation. At the end of an hour the artificially oxygenated infant is only slightly better saturated (91.6 per cent) than the nonartificially oxygenated infant (85 per cent). Six out of the 10 had oxygen saturation levels of 90 per cent or over at the end of one hour. None of the infants in this group required extra oxygen or resuscitation at birth (Figs. 4 and 5).

TABLE VI. REGIONAL ANESTHESIA WITH SUPPLEMENTARY NEONATAL OXYGEN

| | BIRTH | | | 30 MINUTES | | 1 HOUR | |
PATIENT	OXYGEN CAPACITY VOL. %	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION
1	21.0	17.0	81	17.6	84	20.3	97
2	13.9	10.8	78	12.8	92	12.4	89
3	16.7	11.8	71	12.7	76	15.5	93
4	16.1	8.6	53	15.8	98	15.8	98
5	19.2	6.2	32	8.0	42	16.3	85
6	17.2	6.7	39	13.1	76	14.5	84
7	17.3	8.5	49	12.9	75	15.0	87
8	14.8	3.1	21	11.8	80	14.5	98
9	20.1	9.4	47	13.9	69	18.7	93
10	17.8	14.8	83	16.7	94	16.3	92
Average of 10	17.4	9.7	55.4	13.5	78.6	15.9	91.6

7. *Ten Full-Time Infants Whose Mothers Received Ether Anesthesia Five to Twelve Minutes Before Delivery. The Infants Received 60 Per Cent Oxygen Immediately After Delivery. Determinations Done at Birth, One-Half Hour, and One Hour (Table VII).*—

This shows average birth oxygen saturation values at 62 per cent of capacity which is higher than the values when the mother received no general anesthesia. This is because the first samples of capillary blood were taken after 6 out of 10 infants were artificially resuscitated. The delay occasioned resulted in the somewhat higher averages for the first samples. At the end of half an hour, there is no significant improvement in the oxygen saturation values in these infants and at the end of an hour 7 of the 10 infants still had oxygen saturation values below 90 per cent. From this evidence it would appear that giving continuous oxygen for an hour after birth to the infant born of a mother who has had ether anesthesia does not effectively increase his oxygen saturation. Apparently the ether anesthesia interferes with the infant's ability to oxygenate its blood rapidly in a 50 to 60 per cent oxygen atmosphere.

TABLE VII. ETHER ANESTHESIA WITH SUPPLEMENTARY NEONATAL OXYGEN

| | BIRTH | | | 30 MINUTES | | 1 HOUR | |
PATIENT	OXYGEN CAPACITY VOL. %	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION	OXYGEN CONTENT VOL. %	PER CENT SATURA-TION
1	16.9	14.1	83	12.6	75	13.2	78
2	14.6	5.9	40	10.4	71	13.2	90
3	16.0	10.8	68	10.2	64	12.0	75
4	15.4	9.0	58	6.0	39	10.9	71
5	16.0	7.8	49	13.4	84	12.9	81
6	17.0	10.8	64	14.1	77	15.8	93
7	15.3	12.4	81	11.1	73	12.8	84
8	17.2	14.5	84	15.1	88	15.6	91
9	15.3	11.7	77	8.9	58	8.0	52
10	14.9	2.9	20	8.9	60	12.7	85
Average of 10	15.9	10.0	62	11.0	68.9	12.7	80

Comment

The lack of statistically significant differences between the average oxygen saturations of these normal newborn infants both at birth and at one hour may have been due to the small number of infants in each anesthesia series, or
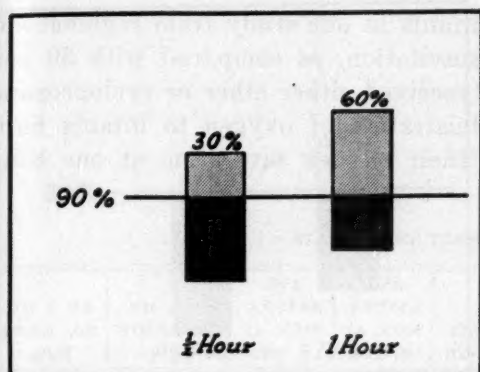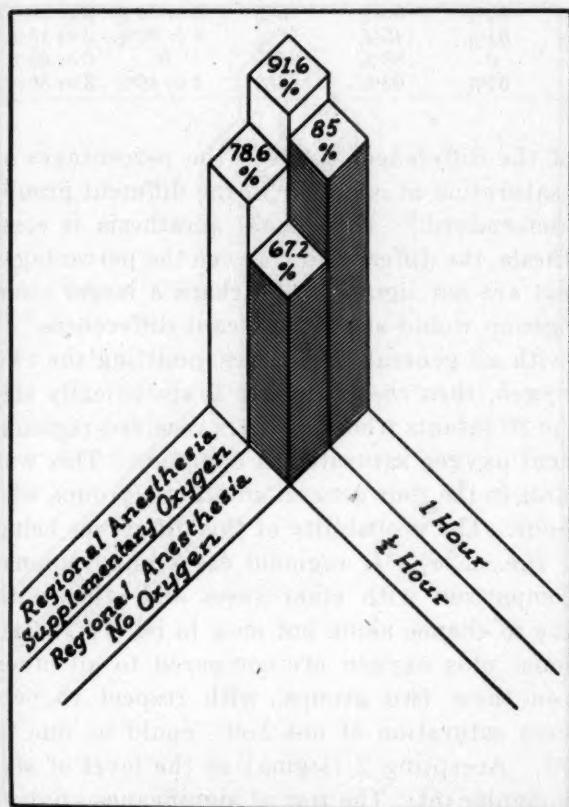
EFFECTIVENESS OF SUP-
PLEMENTARY OXYGEN
WHEN REGIONAL ANES-
THESIA WAS USED.

10 Infants — None Resusci-
tated

½ Hour Saturation — 78.6%
1 Hour Saturation — 91.6%

Fig. 4.- Percentage of Cases Above 90 Per Cent Oxygen Saturation.

REGIONAL ANESTHESIA

Comparison of Neo-
natal Oxygenation
with and without Sup-
plementary Oxygen.

Fig. 5.

to the careful administration and time limitations of the various anesthetics
used. Eastman has shown by his experiments that nitrous oxide anesthesia
for periods of less than 5 minutes in proportions of 85 nitrous oxide to 15 oxy-
gen does not cause harmful neonatal anoxemia.[5] He believes the time element
to be very important. In his study, concentrations of 90 per cent nitrous
oxide and 10 per cent oxygen given longer than 5 minutes produced severe
anoxia of the child in one-third of cases.

We have found that none of the infants in our study from regional anesthesia patients required artificial resuscitation, as compared with 50 per cent of the infants whose mothers had received either ether or cyclopropane (Table VIII). Furthermore, the administration of oxygen to infants born after maternal ether did not improve their oxygen saturation at one hour (Figs. 6 and 7).

TABLE VIII. SUMMARY OF RESULTS

AGENT	NO. CASES	NO. RESUSCI-TATIONS	% RESUSCI-TATIONS	AVG. SATURA-TION AT BIRTH	AVG. SATURA-TION AT 1 HR.	AT 1 HR. NO. BELOW 80%	AT 1 HR. NO. ABOVE 90%
Regional	20	0	0	50%	85%	6 or 30%	9 or 45%
Ether	21	8	38%	60%	79%	10 or 50%	3 or 15%
Nitrous oxide	10	3	30%	43%	81%	5 or 50%	2 or 20%
Pentothal sodium	10	1	10%	50%	80%	3 or 30%	2 or 20%
Cyclopropane	13	7	54%	45%	72%	8 or 62%	2 or 15%
Regional plus oxygen	10	0	0	55%	92%	0	6 or 60%
Ether plus oxygen	10	6	60%	62%	80%	4 or 40%	3 or 30%

The statistical significance of the differences between the percentages of infants who reached 90 per cent saturation at one hour in the different groups (Table VIII, last column) was determined.* If regional anesthesia is compared with any other single anesthesia, the differences between the percentages of infants who reached 90 per cent are not significant; perhaps a larger number of infants in each anesthetic group would show significant differences. If regional anesthesia is compared with all general anesthetics, omitting the two groups who received neonatal oxygen, then the difference is statistically significant. Forty-five per cent of the 20 infants whose mothers received regional anesthesia were 90 or more per cent oxygen saturated at one hour. This was compared to 17 per cent of 53 infants in the four general anesthetic groups who were 90 or more per cent at one hour. The probability of this difference being due to chance alone is one in 35 (i.e., 2.2σ). If regional cases plus regional with oxygen are grouped for comparison with ether cases and ether with oxygen the difference could be due to chance alone but once in 80 (i.e., 2.5σ). Finally, when regional and regional plus oxygen are compared to all other anesthetics the difference between these two groups, with respect to percentages of cases above 90 per cent saturation at one hour, could be due to chance but once in 368 (i.e., 2.9σ). Accepting 2 (sigma) as the level of significance, these differences are all significant. The test of significance applied was that of the differences between percentages:

$$\frac{\text{Difference in \% between compared groups}}{\sqrt{\dfrac{(P)\,(Q)}{n-1} + \dfrac{P_1\,Q_1}{n_1-1}}}$$

This study thus suggests that even with careful administration of general anesthetics to mothers during uncomplicated deliveries, the percentage of

*Statistical analysis by Dr. Lloyd Florio, Department of Public Health and Preventive Medicine, University of Colorado School of Medicine.
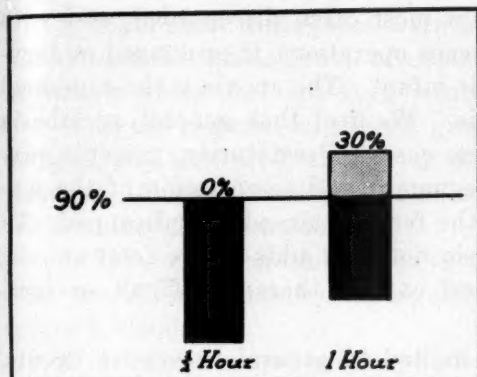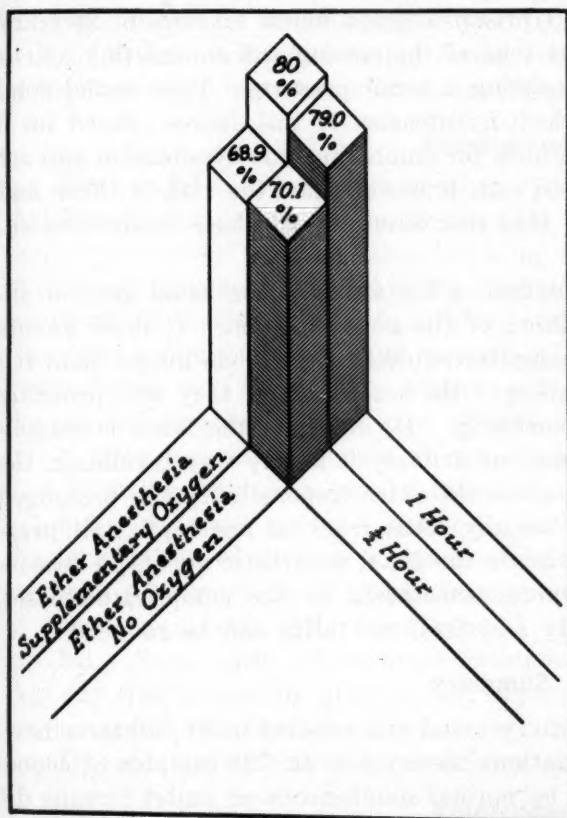
RELATIVE NON-EFFECTIVE-
NESS OF SUPPLEMENTARY
OXYGEN WHEN ETHER
ANESTHESIA IS USED.

10 Infants — 6 Resuscitated

½ Hour Saturation — 68.9%

1 Hour Saturation — 80.0%

Fig. 6.- Percentage of Cases Above 90 Per Cent Oxygen Saturation.

ETHER ANESTHESIA

Comparison of Neo-
natal Oxygenation
with and without Sup-
plementary Oxygen.

Fig. 7.

infants who will reach oxygen saturations over 90 per cent at one hour is significantly higher when regional anesthesia is used than when a general anesthetic is given. Although the effect of the length of anesthesia has not been a part of this study we do believe that it bears a direct relationship to the infant's ability to oxygenate his blood. For this reason we feel that no more than ten or twelve minutes of maternal general anesthesia prior to delivery should safely be undergone by the normal full-term infant. It has been

our observation that this limit in time is most often disregarded, and with regret, at cesarean section. Difficult forceps operations, if prolonged or traumatic, very frequently result in an anoxic infant. The anoxia is the combined result of trauma and general anesthesia. We feel that general anesthesia should be avoided where possible in these cases. Prematurity, placenta previa, placental separation, toxemia of pregnancy, and compression of the umbilical cord are complications in which the fetus is already handicapped. To superimpose the risk of general anesthesia not only adds to the fetal anoxia, but makes extrauterine resuscitation and oxygen therapy difficult or ineffective.

The danger of fetal anoxia is not limited to general anesthetic agents. The maternal blood pressure fall that not uncommonly follows caudal or spinal anesthesia in obstetrics can cause serious fetal anoxia. Hingson and his group[6] stated that if the maternal blood pressure drops below 80 mm. of mercury systolic pressure during labor, the tone of the resting and contracting uterus is conceivably greater than the existing arterial pressure. They found fetal anoxia in almost every case in which hypotension of this degree existed for 5 minutes or longer. There are methods for combating this hypotension and for preventing it. It must be pointed out, however, that the risk is there and only those prepared to deal with that risk should apply these conduction anesthetic methods in obstetrics.

It is our purpose to call attention to the effect of the usual general anesthetic agents on oxygen saturation of the normal infant. If these agents are used in normal full-term uncomplicated deliveries for no longer than ten to twelve minutes at the termination of the second stage, they will probably not increase fetal mortality or morbidity. If, however, the labor is complicated, or the pregnancy is abnormal, or delivery is in any way traumatic, the fetus should not be called upon to share the extra responsibility of a prolonged general anesthetic. The normal healthy fetus from an uncomplicated pregnancy, labor, and delivery can tolerate the usual anesthetic agents in reasonable amounts. By avoiding general anesthesia in the complicated cases, wherever possible, fetal morbidity and fetal mortality can be reduced.

Summary

1. Oxygen saturation of capillary blood was studied in 94 full-term newborn infants. Separate determinations were made on 708 samples of blood. The infants were born vaginally by normal spontaneous or outlet forceps delivery following various forms of maternal anesthesia. Capillary blood samples were drawn at birth, one-half hour, and one hour. In some cases, samples were collected at two, three, twelve, and eighteen hours after delivery. The anesthetics studied were regional, ether with and without neonatal supplemental oxygen, nitrous oxide, cyclopropane, and Pentothal Sodium, all carefully administered for short periods.

2. No statistically significant differences were found between the average saturations at birth or at one hour when a single anesthetic agent is compared with regional anesthesia.

3. Significant differences were found when regional anesthesia was compared with the whole group of general anesthetics with respect to percentage of infants whose one-hour oxygen saturation was above 90 per cent.

4. In the regional anesthesia group, 45 per cent of the infants were 90 per cent oxygen saturated, or over, at one hour of life. In the ether series three hours of life were necessary before a similar number of the infants reached 90 per cent oxygen saturation.

5. The administration of oxygen to the newborn infant after maternal ether anesthesia produced no significant changes in oxygen saturation of the infant's blood.

6. Artificial resuscitation, which was given if respirations were not spontaneously established within three minutes after birth, was required for none of 30 infants born of mothers receiving regional anesthesia. One of 10 infants from the Pentothal Sodium series, 3 of 10 after nitrous oxide, 14, or 45 per cent, of 31 infants from the ether series, and 7, or 54 per cent, of infants born of mothers receiving cyclopropane anesthesia required artificial resuscitation.

Conclusions

The careful administration of ether, cyclopropane, nitrous oxide, or Pentothal Sodium for periods no longer than ten to twelve minutes at the termination of the second stage of labor led to no statistically significant differences in average oxygen saturations of the infants' blood at birth or at one hour when compared to that of infants born after pudendal or saddle block anesthesia. However, a significantly higher percentage of the infants reached saturations above 90 per cent at one hour when regional anesthesia was used than when the general anesthetics were used. Furthermore, no infants required resuscitation after regional anesthesia as compared with from 10 to 60 per cent who died following the various general anesthetics.

Since maternal general anesthesia, given for relatively short periods at the termination of the second stage of labor, tends to prevent the early attainment of normal blood oxygen saturation levels in a significant proportion of newborn infants, prolonged general anesthesia for delivery should be avoided. Some form of regional anesthesia should be used for deliveries that are complicated by prematurity, placenta previa, obstetrical trauma, placental separation, toxemia of pregnancy, or compression of the umbilical cord, since these infants are already candidates for anoxia.

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Discussion

DR. NICHOLSON J. EASTMAN, Baltimore, Md.—In order to understand the unique significance of the work which Dr. Taylor has just presented it becomes essential to recall

the transcendant importance of the period of life he has been studying, the first few minutes. As the late Yandell Henderson remarked a number of years ago, the first 15 minutes constitute the most dangerous period of life because more lives are lost in that interval than in any subsequent month. Immediately after the cord is clamped, the baby is called upon to make an adjustment in his oxygen relationship, or his method of obtaining oxygen, which has no parallel in physiology, and which the baby must accomplish quickly if he is going to survive. The fetus at birth shows a very low arterial oxygen content and an extremely low venous content. This means that the fetus in utero lives continuously in a state of cyanosis with a degree of oxygen unsaturation which would be incompatible with extrauterine life even for a few minutes. Now, in this transition period which Dr. Taylor has studied, he has been following the changes in the fetal blood during these first vital moments of life. He has shown very clearly that general anesthetics handicap this mechanism and retard it. Now some may think that the answer to this difficulty is to go over to conduction anesthesia. He makes note of the fact that this is not necessarily the answer because drops in blood pressure sometimes accompany caudal or spinal anesthesia.

There is one other anesthetic accident which I should like to touch upon from the standpoint of frequency and gravity. I refer to aspiration of vomitus as a cause of maternal death. Drs. Hingson and Merrill of our service sent out 208 inquiries to hospitals in the United States, all hospitals in which there are 2,000 or more deliveries a year, inquiring how many deaths from aspiration of vomitus they had observed in the last 5 years. We had replies from 166 hospitals, covering 2,260,000 births. In these there were 50 maternal deaths from aspiration of vomitus in labor, or 1 in every 40,000 deliveries. Now, the principal warning that these figures afford is that this is a grave threat in patients who have eaten shortly before the onset of labor. In view of these figures there are possibly some who would say that we should go back to giving little or no pain relief. To me this is not the logical conclusion because, by and large, pain relief is beneficial to mother and baby for in any over-all picture it reduces the number of premature forceps operations. Pain relief should be used in sparse dosage. The time element is very important and the timing of the analgesia and the anesthesia should be such as to allow the fetus to receive as little as possible. In addition, eternal vigilance is necessary in cases of caudal and spinal anesthesia to watch for blood pressure drops; and in cases of general anesthesia or prolonged anesthesia, it is necessary to be ever alert in regard to the possibility of vomiting. Finally, another lesson to be drawn from this paper is that research in this field, as emphasized by this paper by Dr. Taylor, should go on with increasing zeal to the end that we may eventually have drugs and techniques which will make anesthesia completely safe as well as efficient.

DR. WILLIAM F. MENGERT, Dallas, Texas.—This paper represents a sincere attempt to adduce laboratory proof of clinically recognized human phenomena. The authors are to be congratulated for their method of approach to the subject, and for focusing our attention again upon the relation of anesthetic agents to fetal hypoxia, although lowered fetal oxygen values are generally disregarded, they are none the less a real hazard of childbirth.

That this hazard is introduced by the attendant, and is not naturally a part of the birth process, makes it all the more significant. This is not to say that we should immediately return to primitive conditions and allow all children to be "born in sorrow." It is intended to say that we should choose our anesthetic agents carefully with due regard for the patient, the dangers involved, and the exigencies of the situation. The time is long since past when a conscientious physician, his arrival at the birth room delayed, can permit the house staff to anesthetize the mother in an effort to retard the progress of labor. Other misuses of anesthetic agents are familiar to us all.

Although figures, standards and statistical methods of calculation vary, it would seem reasonable to state that the principal, over-all cause of fetal death before, during, and immediately after birth is oxygen deprivation. How much, if any, damage results in the survivor of a period of lowered oxygen content, is unknown.

There is virtual unanimity of recorded opinion, so ably expressed by Beck, "Most of the methods which have been recommended for the relief of pain during labor may cause the death of the child if they are not given with caution."

Once again we should pay tribute to the authors of this interesting and informative presentation for emphasizing that maternal anesthetic agents temporarily depress the oxygen content of the blood of the newborn, and in some instances delay recovery to average levels.

Oxygen content under an ether mask is often reduced to levels as low as 15 per cent. One wonders what would have happened to the babies whose mothers received drop ether, if oxygen had been delivered under the mask by means of a soft rubber catheter. In other words, was the delayed return to normal due to the ether or to hypoxia?

Cyclopropane is a powerful and quick-acting anesthetic agent. By "pushing" its administration it is possible to attain high blood concentrations with only a few respiratory interchanges. It would, therefore, be desirable to know what anesthetic plane was reached in these various patients. In other words, unless the plane of the anesthetic was identical in the various women of the study, their subsequent behavior is not comparable. No matter what inhalation anesthetic agent is employed, fetal embarrassment will often follow descent of the mother into the third plane of anesthesia.

DR. T. L. MONTGOMERY, Philadelphia, Pa.—I would simply like to add my favorable comments to those of the discussants concerning this excellent and original presentation. I believe, of all the papers listed, this seemed to me the most timely and the one I would be most interested in because I believe it represents the major problem in obstetrics today, and one of the many problems responsible for high fetal morbidity and mortality. Several of the questions I have in mind have already been projected. I would be interested in knowing whether administration of ether was continuous or whether it was interrupted. Also, I think we are interested in knowing whether the anesthetic agents depress fetal oxygenation due to the anesthetic agents crossing the placenta, or by primary depression of the oxygen content in the maternal blood and a relative depression of oxygen of the fetus in utero. Those are very important considerations, and I would like to know whether Dr. Taylor has run any controls in the series of Demerol 1 to 3 hours, and babies without Demerol, because we know that in the weak and premature fetus even introduction of 100 mg. of Demerol within 1 hour of delivery may greatly depress the centers; it must be somewhat true of the full-term infant, and perhaps the effect, plus the inhalation anesthesia, may be an important consideration.

DR. F. E. WHITACRE, Memphis, Tenn.—In our hospital in the past two or three years we have been working on a problem along similar lines. Encephalographic tracings are made on the newborn soon after delivery, a few hours later, and a few days later. Dr. James G. Hughes of the Department of Pediatrics has reported on various drugs in common use. In general the findings show that they are all depressing. Delvinal, of the barbiturates, seems to be the greatest offender, and of the other drugs Demerol seems to be the least offender.

DR. TAYLOR (Closing).—The discussants have raised interesting questions; many I cannot answer. I think it is important to realize that all work that is being done in this field has as its base line the original work of Dr. Eastman on oxygen saturation. It is of interest that an adult subjected to blood oxygen saturation of 65 to 70 per cent will be rendered unconscious. Newborn infants can live at a much lower saturation than this during the first few hours of life and not become unconscious. I am pleased that Dr. Mengert emphasized the point of the prolonged anesthesia and the sin of having the patient being long anesthetized while the doctor is brushing up his office affairs before he goes to the hospital for the patient's delivery.

Our patients were anesthetized to the point where they could be delivered by episiotomy and low forceps operation, but no deeper. In other words, they were not placed

in the third plane of anesthesia before the delivery occurred. These patients did not receive a continuous flow of oxygen through a mouth tube while being anesthetized with open drop ether.

Dr. Montgomery brings up the question as to whether the anesthetic agents depress fetal oxygenation due to the anesthetic agents crossing the placenta, or by primary depression of oxygenation in the maternal blood. We have no conclusive studies that will answer this important question. We did analyze the blood of the mother and her child for oxygen saturation in a few instances, and our tentative conclusion was that the small amounts of anesthesia given to the mother did not materially reduce her blood oxygen saturation. We believe the major depressive action is the presence of the anesthetic agent in the blood of the infant, although we have no positive proof. After starting this work we did think it might have been a better controlled experiment had Demerol and hyoscine been eliminated as premedication drugs. However, one of our purposes was to conduct an experiment that would measure the oxygen saturation of newborn infants born under the usual hospital analgesic and anesthetic program. In further experiments we intend to measure the effect of each drug, according to its separate action.

I think Dr. Whitacre's work is very important, and it should be correlated with the effects of agents used for relief of pain in obstetrics.

ETIOLOGY OF HEMORRHAGE IN PLACENTA PREVIA*

DAVID FINDLEY, M.D., OMAHA, NEB.

(From the Department of Obstetrics and Gynecology, University of Nebraska, College of Medicine)

FOR years we have been led to believe that the unavoidable hemorrhage associated with placenta previa was on a purely mechanical basis. This theory, formulated by our predecessors, however, does not meet the test of time in many cases. Bleeding frequently occurs during the second and early stages of the third trimester of pregnancy, before these various mechanical factors can enter the picture. In these patients, particularly, other predisposing etiological factors must be sought for and recognized.

As is well known, placentation normally takes place well up on the uterine wall and far distant from the internal os of the cervix. The decidual reaction in this area is far better developed than in the lower uterine cavity, as is the local blood supply, and thus invites implantation of the embryo. Many conditions may occur, however, which will prevent normal placentation.

Defective vascularization of the decidua as a result of inflammation or atrophic changes resulting from repeated pregnancies are among the more common causes. Neoplastic formations which encroach upon the uterine cavity and congenital malformations may prevent implantation in the upper portions of the uterus. Such atrophic changes naturally would limit the blood supply to the placenta. Therefore, the placenta must spread out its attachment and may thus border on, encroach upon, or cover over the internal cervical os. Hofmeier's theory, that of the development of the placenta in the decidua reflexa, must also be recognized as an etiological factor in placenta previa. During the latter weeks of pregnancy the lower uterine segment becomes thinned out, the cervix becomes effaced and dilated to some degree. As a result of this stretching the placenta is partially torn from its attachment with resulting hemorrhage. The mechanical process is undoubtedly the causative factor of bleeding in the great majority of cases, but by no means in all.

Trauma may play an important role as an exciting factor in the production of bleeding in placenta previa. Unwarranted, repeated, or vigorous pelvic examination, either per rectum or vaginam, or coitus may produce hemorrhage of excessive degree. Such hemorrhage, however, is due to separation or penetration of the placenta and is also on a mechanical basis. Any or all unnecessary pelvic manipulations, especially in the face of abnormal bleeding, should be avoided.

Material

In a series of 6.921 consecutive patients delivered in the Nebraska
Methodist and the University of Nebraska Hospitals over a five-year period
placenta previa was recognized 32 times, or a ratio of 1 in 216 deliveries.
Fourteen, or nearly one-half of these patients presented symptoms before the
thirty-sixth week of gestation, before effacement or dilatation of the cervix
would normally occur. All of the pregnancies were terminated immediately
upon the recognition of the previa. Seven, or 21.7 per cent, of the babies were
lost. Three of these pregnancies were terminated before the twenty-eighth
week and the fetuses were considered nonviable. This leaves a corrected fetal
mortality rate of but 12.5 per cent. There were no maternal deaths. Central
placenta previa was found 8 times, partial 10 times, lateral 9 times, and in 5
cases classification was not noted. Twenty-three patients were delivered by
cesarean section with 5 fetal deaths and 9 through the vaginal route with 2
infant deaths.

Fig. 1.—Cross section of uterine wall and placental margin, showing relation of sinus to normal
separation plane and to membrane reflection.

Of these, 10, or nearly one-third of the cases, showed definite evidence of
hypertensive toxemia associated with albuminuria. Although the records
were incomplete, the majority of the placentas examined showed extensive
areas of infarction, thus further evidence of toxemia. The placental pathology
observed appeared identical to that found so frequently in abruptio placentae.
It would seem logical to assume therefore that the bleeding in many cases of
placenta previa, especially those seen before the thirty-sixth week of gestation,
is due to a disturbance of placental circulation with resulting necrosis of the
decidua basalis and separation from the site of implantation. ·

During the same five-year period abruptio placentae was diagnosed 20 times or an incidence of 1 to 346 deliveries. Five of these cases, or 20 per cent, were terminated before the thirty-sixth week of gestation, the remaining 15 from the thirty-sixth week to term. There were 9 fetal deaths, an incidence of 45 per cent. Three of these fatalities occurred before the twenty-eighth week of pregnancy. This leaves a corrected fetal mortality rate of 30 per cent. There were no maternal deaths. Ten patients were delivered by cesarean section with 4 fetal deaths and 10 through the vaginal canal with 5 deaths. Six were primigravidas and 14 multigravidas. Eight, or 40 per cent, showed definite evidence of hypertensive toxemia.

Although these two series of cases are extremely small, I feel that they are representative of these pathological conditions and that certain conclusions may be drawn from the above analysis. Toxemia, of the hypertensive type, was noted in a large percentage of cases both in placenta previa and in abruptio placentae. The majority of patients were multigravidas. Placental pathology proved identical in both conditions in the majority of tissues examined. Trauma played a negligible inciting role in both. The fetal mortality rate was high in both series, there were no maternal deaths in either. The method of delivery varied with the individual patient's condition and physical findings.

In review of the above discussion certain cases of placenta previa, as well as abruptio placentae, might be avoided by early recognition and correction of congenital abnormalities, the removal of neoplasms, the prevention of puerperal infection, and the proper spacing of children. Strict supervision of the pregnant patient, especially those with hypertensive toxemia and allied symptomatology, might help to annul early hemorrhages and more pregnancies will be carried closer to term with a lessened fetal mortality rate.

Summary

The generally accepted theory that hemorrhage in placenta previa results purely from mechanical separation of the placenta following the development and formation of the lower uterine segment, effacement or dilation of the cervix, or following intravaginal manipulation must be disregarded. This is evident because many a patient presents symptoms during the seventh or eighth month of pregnancy before these mechanical factors become apparent. Many other factors must be considered. Faulty implantation of the placenta, endometritis, or neoplastic formation must be included as possible etiological factors in the production of uterine hemorrhage. Careful prenatal supervision will help to reduce the incidence of pre-eclampsia and may thus help to carry more patients closer to maturity before the unavoidable bleeding of placenta previa occurs.

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Discussion

DR. E. D. COLVIN, ATLANTA, GA.—I cannot agree with Dr. Findley that "the development and formation of the lower uterine segment, effacement or dilation of the cervix, or intravaginal manipulation must be disregarded" as etiological factors in the hemorrhage of placenta previa. I do believe that any one or combination of the aforementioned factors may serve as an inciting cause in the production of such a hemorrhage.

As to the exact origin of bleeding in placenta previa hemorrhage, I very strongly believe that modern obstetric writers have failed to place the proper emphasis on an anatomic

structure which possibly is the origin of hemorrhage in many cases of placenta previa, the
marginal sinus of the placenta. Jacquemier in 1839, J. Mathews Duncan in 1875, and Budin
in 1896 included rupture of the marginal sinus as one of the sources of bleeding in placenta
previa and recognized that rupture of the sinus also occurs when the placenta is normally
situated.

Practically every obstetrician of experience, in performing cesarean section for placenta
previa, has experienced the embarrassment of having found the placenta, not in the lower
segment, but attached high in the uterus. Upon the removal of the placenta, its gross appear-
ance with attached blood clot at the edge extending over the maternal surface of the
adjacent cotyledons and the membranes is almost identical to the picture found in placenta
previa.

Through close examination of all placentas we have come to the realization that rupture
of the placental blood channel known as the marginal sinus is responsible for many hemor-
rhages erroneously diagnosed as due to placenta previa, abruptio placentae, or causes un-
known.

The marginal sinus is situated at the edge or just within the periphery of the marginal
cotyledons, beneath the closing ring of Waldeyer, and is often involved in the fibrous chorionic
and decidual degenerative concentrations at this site. It is intermediary between the periphery
of the subchorionic maternal blood space and the uterine sinuses of the belt zone of the
decidua basalis, into both of which many communicating openings are demonstrable on its
medial and inferior walls. Variations in caliber and thickness of the walls of the sinus are
probably dependent on its involvement and the location of the marginal closing of the placenta.
The excellent dissections of Rudolph Spanner of in situ placental specimens indicate that the
marginal sinus bears fundamental importance to the circulation of the intervillous space of
the placenta.

It is conceivable that formation of the lower uterine segment late in pregnancy may so
disturb the low placenta that rupture of the marginal sinus as well as or instead of separa-
tion of a cotyledon, may occur, with the result that blood spreads out over the membranes,
separates the maternal surface of adjacent cotyledons, escapes through the cervix, and forms
a clot locally adherent at the site of rupture on the placental margin.

So often, examination of the area involved by the clot alone fails to enable one to
differentiate between bleeding due to placenta previa and that of rupture of the marginal
sinus or abruptio placentae. In the latter, it is our belief that the high incidence of clinical
evidence of toxemia along with uterine findings and the ability to demonstrate acute infarction
in the formalin-fixed placenta enables one to establish a diagnosis of abruptio placentae.

From a clinical viewpoint, it is important to keep in mind that extensive hemorrhage in
the last trimester of pregnancy may be due to conditions other than placenta previa. Un-
fortunately, diagnosis is not always possible. If vaginal confirmation is omitted in selecting
cases for expectant treatment, when placenta previa is suspected, consideration must be
given in regard to bleeding due to true previa and ruptured marginal sinus in cases of normal
implantation of the placenta on the one hand, and abruptio on the other. There obviously
exists no expectant treatment for abruptio placentae since this condition terminates pregnancy.

In an unpublished study, by Dr. John S. Fish, of 2,655 gravidas delivered consecutively
by the Bartholomew Group, there were found 147 cases of third trimester hemorrhage, or
hemorrhage in labor of such an amount as to be of concern to the attendant. Fifty-one, or
34.6 per cent (17 proved), were attributed to placenta previa; 50, or 33.9 per cent, resulted
from a rupture of the marginal sinus in normally implanted placentas, and 14, or 9.6 per cent,
accompanied abruptio placentae. In regard to the clinical behavior of hemorrhage due to
placenta previa and rupture of the marginal sinus in normally situated placentas, Dr. Fish
made certain deductions, some of which are: (1) placenta previa showed a greater tendency
to recurrence of bleeding, also a higher incidence of bleeding before labor (49 per cent)
than rupture of the marginal sinus (30 per cent), (2) in antepartum hemorrhage, rupture
of the marginal sinus was attended by gross hemorrhage in 73.3 per cent, placenta previa in
56 per cent, (3) ruptured sinus bleeding was more often associated with labor (58 per cent),

apparently due to the irritation of retained blood and clots higher in the uterine cavity, (4) the blood of ruptured sinus and placenta previa was bright red, but in abruptio it was more often a dark color, (5) evidences of toxemia were associated with abruptio placentae in 64.3 per cent, with ruptured marginal sinus in 8 per cent, and with placenta previa in 1.9 per cent, (6) the fetal mortality in placenta previa was 9.8 per cent, in abruptio placentae 28.6 per cent, and in ruptured marginal sinus 4 per cent.

At the present time, it is my belief that, in all probability, the high degree of success attributed to the expectant plan of treatment of placenta previa, in the absence of vaginal examination, truthfully, but unknown, is the result of inclusion of a high percentage of hemorrhage cases labeled as placenta previa but due to blood loss from a rupture of the marginal sinus in normally implanted placentas.

CARCINOMA OF THE CERVIX UTERI DURING PREGNANCY, WITH SPECIAL REFERENCE TO COMPARISON OF SPONGE BIOPSIES WITH DIAGNOSTIC PAPANICOLAOU SMEARS*

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IN A previous study of 2,264 cervices of pregnant women chiefly by haphazard biopsies, concluding by 222 Papanicolaou smears, we[1] found 2 cancers (0.09 per cent). This is double the average previously reported incidence, therefore it seemed reasonable to continue the investigation, if only to establish the frequency of cervical cancer during pregnancy in so far as it can be done by cytologic screening methods.

Recent reports following completion of our preliminary study show interest in the subject, but as yet no apparent systematic use of cervical smears or the newer sponge surface biopsies. W. O. Johnson and Weinfurtner[2] quote an average incidence of cervical cancer in pregnancy of 0.056 per cent from 18 authors and report 12 cases (0.04 per cent) among 29,394 obstetrical patients in the Louisville General Hospital, in addition to 2 cases of carcinoma in situ. Kauffmann, Cuyler, and Ross[3] via smear screening found 44 cases of intraepithelial cervical cancer representing 0.44 per cent of 10,029 patients in the Obstetrical-Gynecological Department, Duke University Hospital, 6 of the 44 being found in pregnancy.

Vara[4] found only 18 cervical cancers (0.020 per cent) among 90,644 obstetrical cases in the Women's Clinic of the University of Helsinki, while Paracchi[5] reports 17 personal cases from an unknown total number of patients.

As will be shown later, in this present study, we found one more very early cancer of the cervix through 1,169 smears and 241 sponge biopsies (0.06 per cent), or a total in 2 studies of 3 malignancies (0.075 per cent) among 3,674 pregnant women. Consequently, we feel justified in discussing certain practical aspects of cervical cancer detection during the pregnant state.

Availability of Subjects.—Since 90 to 95 per cent of all pregnant women receive some prenatal care, and since pregnancy and recovery spread over nearly a year, neglect of some sort of critical attention to the cervix is certainly not in line with modern trends.

Subjective Symptoms.—Common bleeding and discharge during pregnancy may well be due to neoplasm, and, on the contrary, most very early cervical cancers cause no symptoms.

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*Read at the Sixty-first Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 7, 8, and 9, 1950.

Objective Signs.—The gross appearance of the pregnant cervix is usually markedly altered as to consistency, size, color, friability, and "erosion," but there seems to be less agreement on macroscopic than on microscopic changes. For convenience, we designated crude groupings and found two-thirds of our Preston Maternity present series of cases strikingly abnormal.

TABLE I. CLINICAL GROUPING OF 446 PREGNANCIES ACCORDING TO GROSS CERVICAL
APPEARANCE

No disease		150
Erosion		294
Simple	101	
Elevated	20	
Papillary	169	
Cystic		15
Polyps		7

At least one-half of the above nonmalignant cervices required cytologic screening to rule out tumor.

Status of Cervical Cytology and Biopsies in Pregnancy

From our own experience, we believe that both smear and sponge cytology are as accurate as in the nonpregnant patient, and especially appropriate; and that punch, but *not* sharp conization or ring tissue biopsies, is both safe and reliable.

Kaufman and Fiege[6] from 1,721 nonpregnant patients in general office practice, mostly via vaginal smears, found 47 positive specimens (2.7 per cent) of which 26 were proved malignant by curette or biopsy.

A clinical evaluation of 3,500 vaginal cytologic studies in the Department of Gynecology of Syracuse University College of Medicine by Reicher, Massey, and Bechtold[7] revealed 85 cases of genital cancer among which were 67 squamous-cell cervical tumors yielding 5.9 per cent false negative and 14.9 per cent false positive tests. This compares favorably with Lock and Caldwell's[8] discovery of 165 cases of cervical cancer from 1,797 biopsies in 10,014 nonpregnant clinic visits.

Piper[9] reports 19 preinvasive cervical cancers (2.5 per cent) among 739 cervical carcinomas in Mayo Clinic from 1940 to 1944, and 11 (0.68 per cent) preinvasive cancers from 1,600 office biopsies. Younge, Hertig, and Armstrong[10] from biopsies of all eroded, everted, or Schiller-positive cervices found 135 carcinomas in situ (1.2 per cent), with average age of patients 9 years less than age in invasive cancer cases. Vaginal smears by these 3 authors showed 71 per cent accuracy in first or second smear, but 93 per cent accuracy in cases of gland or early stromal involvement, which contrary to Te Linde, Novak, and Meyer were not considered invasive.

In the Strang Cancer Prevention Clinic of Memorial Hospital by routine vaginal and cervical smears from 8,000 asymptomatic women, Skapier[11, 12] verified 22 positive smears of early cervical cancer. From 115 proved uterine malignancies among 5,314 general hospital admissions, institutional inmates and city patients, Kraushaar, Bradbury, and Brown[13] found 88 per cent of the *first* vaginal smears to be positive.

Technically, Graham and McGraw[14] have demonstrated increasing accuracy of vaginal cytologic smears for squamous-cell cancer, but limitations for adenocarcinoma; while Graham and Meigs[15] by 8,131 *initial* smears from 401 squamous-cell and 31 adenocarcinomas of the cervix, diagnosed 90 per cent of the tumors, plus 87.5 per cent of 40 cases of carcinoma in situ, with a

false negative error of about 10 per cent and a false positive error of only 0.04 per cent in the most recent cases.

Many authors have found that the cervical smear readily picks up pre-invasive cervical cancer from the nonpregnant woman, and Nieburgs and Pund in reporting 22 preinvasive and 4 borderline cancers of the cervix describe exfoliation of specific malignant cells showing irregular bordered hyper-chromatic or foamy agranular nuclei.

A new method of surface cervical biopsy was introduced by Gladstone in 1948[17] featuring paraffin block preparations of small bits of gelatin sponge after it has been soaked in fluid from, and rubbed on surface tissue of breast cervix, lungs, and rectum. Later[18, 19] the same author secured results com-parable to Papanicolaou smears with the advantage of relatively simple fixa-tion, staining, and microscopy. More recently, Rich, August, and Carpenter[20] (Queen's Hospital, New York City) by this method found no false positive tests in 68 nonpregnant women and 6 false negative slides from 15 definite uterine carcinomas.

Limitations of Cervical Tissue Biopsy in Pregnancy

Suspicious or positive cytologic readings by either test must be followed by tissue biopsy, but only by minute multiple "punches," and *not* by ring specimens or sharp conization followed by coagulation, because of the danger of hemorrhage, abortion, or infection. This precludes examination of the entire squamocolumnar junction area, and therefore determination of the precise ex-tent of presumptive carcinoma in situ as well as positive differentiation from possible marginal portion of invasive cancer or microscopic invasive cancer. However, repeated cytologic examinations and small multiple punch biopsies are safe and should fairly well indicate the process if time permits.

As to microscopic reading of cervical tissue punches, histologic pregnancy changes (mainly decidual reaction, epidermization, and hyperactivity of basal-cell layer) have not apparently confused our pathologists any more than the frequent appearance of histiocytes in the smears.

Mechanism for Processing Cytologic and Tissue Specimens*

Papanicolaou smears from the cervices of pregnant women were secured in the usual manner, but cervical tissue biopsies were limited to punch speci-mens followed by sulfonamide powder applied on cotton pressure ball and not by coagulation.[1] Gladstone's method of taking gelatin-sponge surface bi-opsies was followed precisely, with the use of a ring sponge holder for ap-plication and for rubbing the cervix, with ample time allowed for soaking.

TABLE II. PAPANICOLAOU CERVICAL SMEARS, PRESTON MATERNITY HOSPITAL, JUNE 1, 1949, TO JAN. 5, 1950

Negative	208
Suspicious	3
Positive	0

Punch biopsies of 4 negative and 3 suspicious cervices showed no car-cinoma. Only 2 smears were unsatisfactory and repeated.

TABLE III. GELATIN SPONGE CERVICAL BIOPSIES, PRESTON MATERNITY HOSPITAL,
JAN. 1, 1950, TO JULY 26, 1950

Negative	232
Suspicious	3
Positive	0

Punch biopsies of 3 negative and 3 suspicious cervices were negative for car
cinoma. Twenty sponge biopsies were unsatisfactory and repeated.

TABLE IV. PAPANICOLAOU CERVICAL SMEARS, PHILADELPHIA GENERAL HOSPITAL,
JUNE 1, 1949, TO JULY 1, 1950

	SMEARS	BIOPSIES		
Class I	939	0		
Class II	13	13	"No malignancy"	1
			Chronic cervicitis	12
Class III	5	5	Acute and chronic cervicitis	1
			Chronic cervicitis	4
Class IV	1	1	Bowen's disease	
Class V	0	0		

The above 958 smears plus previously reported 157 negative smears, revealed
1 cancer in 1,115 pregnancies from this hospital.

TABLE V. DIRECT COMPARISON OF GELATIN SPONGE BIOPSIES AND PAPANICOLAOU CERVICAL
SMEARS, PHILADELPHIA GENERAL HOSPITAL

SMEARS	NEGATIVE SPONGE BIOPSIES	PUNCH BIOPSIES
Class I	32	0
Class II	4	3 (chronic cervicitis)
Class III	1	1 (chronic cervicitis)
Class IV	1	1 (Bowen's disease)
Class V	0	0
Class ? (no smears)	6	0

No false positive sponge biopsies from 44 pregnancies showing 1 positive
smear (Bowen's disease).

Dormant Period of Carcinoma in Situ and Occult Period of Invasive Cervical Cancer

The first has been proved extremely variable, probably averages 5 to 6
years or more, and the second *may* also be a matter of years. Therefore, the
childbearing age should show a fairly high incidence of cervical cancer and
certainly pregnancy is not protection against the disease. This assumption
would seem to be refuted by the low incidence of pregnancy cancer reported
from even our largest and best prenatal clinics, but it is supported by our small
series of systematically studied cases and we feel sure will be confirmed.

Management of Cervical Cancer During Pregnancy

We trust that frequent use of cytologic screening will produce large
enough series of cases to indicate ideal treatment, but meanwhile one must
depend upon collective opinions and limited personal experience. The solu-
tion is further complicated by debatable aspects of preinvasive cancer, rela-
tive merits of radical surgery as accomplished by Meigs versus the apparently
irreducible irradiation results as effected by Corscaden, to which are added
profound pregnancy changes.

Galvin and Te Linde[21] consider noninvasive cervical cancer as true cancer.
In their study of 75 patients, 68 of whom were operated upon (some with con-
servation of one ovary) and 7 irradiated, 55 showed microscopic invasive can-
cer. One of the 7 irradiated patients died.

On the other hand, five-year follow-up by Younge, Hertig, and Armstrong[10] of 69 cases of preinvasive cancer involving only the surface epithelium (which cannot positively be determined in pregnancy), treated only by coagulation or excision, showed 85 per cent cure. The remaining 15 per cent later showing carcinoma in situ and treated by simple total hysterectomy gave combined 100 per cent cure. Also, W. O. Johnson[2] reports 2 cases, neither treated, each subsequently delivered and one well after 16 years' observation.

Conservatively, Ayre[22] reports 2 patients with preinvasive cervical cancer completely removed, as proved by ring biopsy and coagulated, they were then allowed to conceive after rigid follow-up. Furthermore, it is fairly common experience for the cervix to show no trace of cancer after complete hysterectomy following positive diagnosis of carcinoma in situ by generous biopsies with or without cauterization (Piper).

Ayre[23] also reports behavior of 7 cases of preinvasive cervical cancer in nonpregnant patients, discovered by a modified technique of surface-biopsy scraping, 6 of which progressed to invasive cancer in 6 to 18 months, and one showed no progression after 18 months, or in other words none regressed.

It would seem proper at the present time to handle carcinoma in situ conservatively during pregnancy with repeated cervical cytologic tests and punch biopsies, followed by postpartum ring biopsy and coagulation or conization.

As to invasive cervical carcinoma discovered during pregnancy, treatment depends upon the stage (*not* the grade) of malignancy and the duration of the pregnancy, without delay in favor of the infant, and in our judgment without palliative cervical and/or vaginal radium application preceding later birth.

Pending improved diagnosis, no single clinic at present can formulate ideal treatment. However, it is apparent that, although x-ray followed by radium for early-stage cervical cancer in early pregnancy will give results comparable to that obtained in nonpregnant women, there is a tendency toward radical surgery. Hysterotomy is not essential, but if elected, then Wertheim's operation can be done simultaneously, or following posthysterotomy irradiation. Obviously, discovery of early cervical cancer in late pregnancy indicates cesarean section or cesarean hysterectomy followed by irradiation, possibly still later by radical surgery.

There is general agreement that late cervical cancer requires, depending on duration of pregnancy, hysterotomy or cesarean section, usually with coincident subtotal hysterectomy, and prompt x-ray and radium exposure, with avoidance of vaginal delivery.

Case Report

M. H., a 21-year-old Negro woman, gravida ii, para i, registered in the prenatal clinic of the Philadelphia General Hospital Sept. 29, 1949, in the seventh month of pregnancy. General physical examination was essentially negative and pelvic examination revealed a cystic but well-epithelized cervix. A routine Papanicolaou smear was taken of the cervix and this was read as Grade IV (positive for malignant cells).

On November 12, re-examination showed an innocent-appearing cervix, the examiner being at a loss as to where to take a biopsy. Therefore punch biopsies were taken from the squamocolumnar junction of the cervix corresponding to three, six, and nine o'clock. Several of the biopsy specimens were covered by epithelium showing epidermoid metaplasia and in one location there was a sharp transition between normal cervical epithelium and metaplastic epithelium. Projecting from the metaplastic epithelium was a small exophytic nodule covered by similar epithelium and containing nests of atypical, definitely anaplastic, squamous cells, each surrounded by basement membrane. Atypical mitoses were seen.
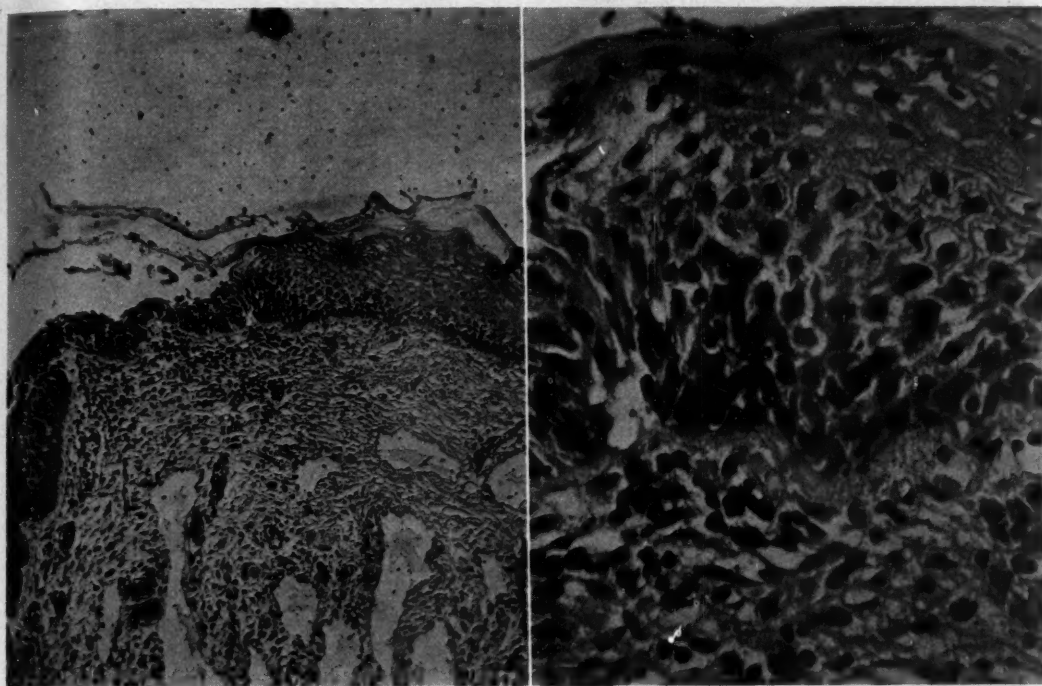
A.

B.

Fig. 1.—Photomicrographs from biopsy of asymptomatic questionable early invasive cancer of cervix in late pregnancy. A. Low power. B. High power.
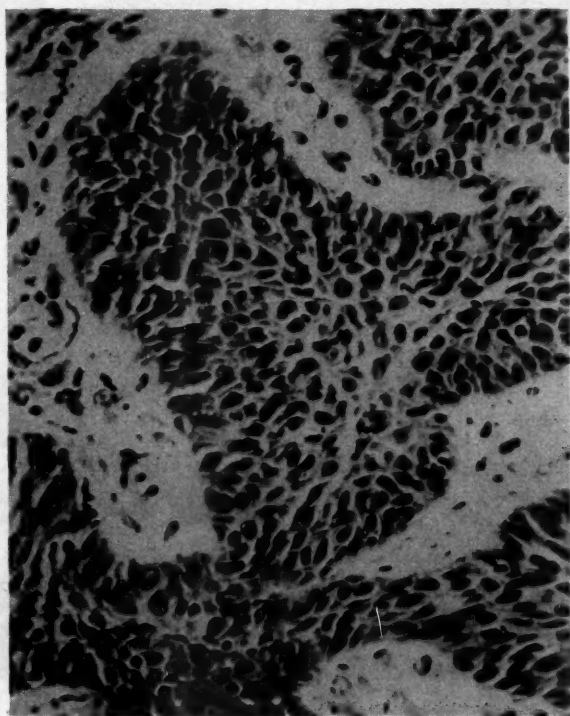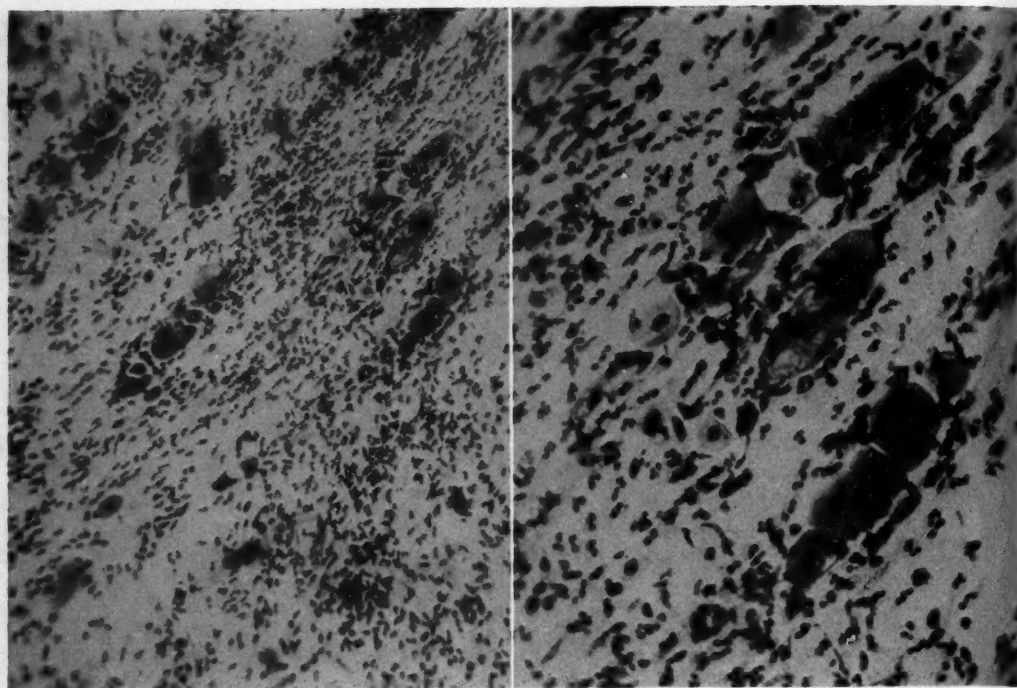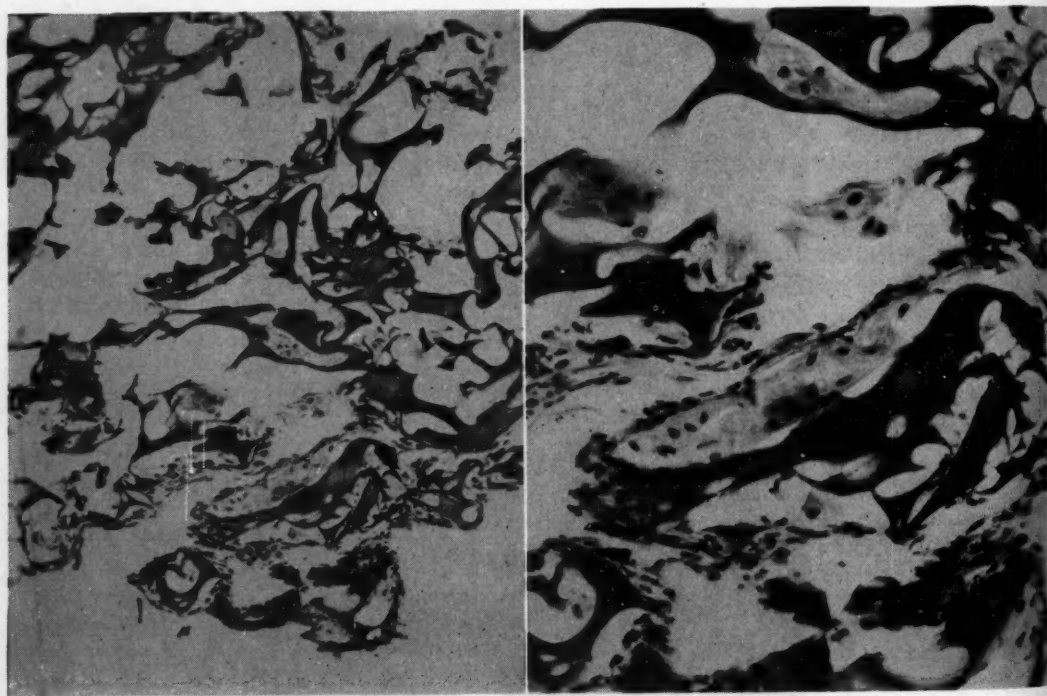

Fig. 2.—Photomicrograph from biopsy of asymptomatic questionable early invasive cancer of cervix in late pregnancy.

Fig. 3.—Photomicrograph of Class IV Papanicolaou cervical smear from cystic cervix, positive for squamous-cell cancer in late pregnancy. A. Low power. B. High power.

Fig. 4.—Photomicrograph of negative gelatin sponge biopsy from questionable early invasive cervical cancer in late pregnancy, taken on seventh postpartum day. A. Low power. B. High power.

The stroma of the nodule showed a decidual reaction, but there was no invasion of the submucosa by the tumor. The pathological diagnosis was Bowen's disease; early exophytic intraepithelial epidermoid carcinoma.

On Nov. 16, 1949, the patient was admitted to the hospital in active labor, and six hours later delivered a 5-pound 15-ounce normal male infant without difficulty. Her postpartum course was uneventful except for a slight mastitis which caused fever on the third postpartum day. On the seventh postpartum day Gelfoam sponge biopsies were taken from the cervix which presented a normal postpartum appearance. Abundant mucus, leucocytes, and some desquamated epithelial cells filled the interstices of the sponge, but malignant cells were not identified.

It was decided to operate upon this patient rather than to use radium and x-ray and accordingly on Dec. 1, 1949, a panhysterectomy and bilateral salpingo-oophorectomy were performed. Her postoperative course was uneventful and she was discharged to the outpatient department for follow-up on her twelfth postoperative day.

Pathological examination of the operative specimen revealed chronic inflammatory infiltration of the cervix, but no evidence of malignancy. Serial sections of the cervix also failed to reveal carcinoma. The uterus showed evidence of the recent pregnancy. The tubes and ovaries were essentially normal.

Conclusions

1. For reasons of availability of subjects, prolonged dormant or latent period of very early cervical cancer, reasonable dependability and safety of methods, and frequency of confusing gross changes, cervical cytologic screening is especially valuable during pregnancy.

2. Papanicolaou smears of the pregnant cervix yield more false positive, and gelatin sponge biopsies, more false negative readings.

3. Early cancer of the cervix in pregnancy occurs much more often than reported through ordinary prenatal examination, viz., 0.09 per cent in our first series and 0.06 per cent in the present series of cases, totaling 3 cases among 3,674 pregnancies, of which 1,632 were screened by cytologic methods (incidence of cancer 0.075 per cent).

4. Management of cervical cancer depends upon the stage of the disease and the duration of pregnancy.

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Discussion

DR. W. G. COSBIE, Toronto, Ont.—The association of a major vital process and a major pathological process will always provide the basis for an interesting subject and so we have seen numbers of papers on carcinoma of the cervix associated with pregnancy. It is also true that the use of the vaginal smear has resulted in an extensive literature. To the best of my knowledge, however, I think that Dr. Hirst is the first to report on the screening of a large number of pregnant women in a search for early cancer. I wish to congratulate Dr. Hirst on a most interesting paper. To me it has been very thought provoking.

Well-developed cancer is as easy to recognize in the pregnant as it is in the non-pregnant cervix, if we look for it. The same is not true, however, in the early phases of malignant disease. The physiological changes in the pregnant cervix are responsible for an appearance which may readily mask an area of tumor and as a result it is easy to take a biopsy from the wrong situation. I agree, therefore, with Dr. Hirst that a suction smear or surface scrape is of definite value. It is only natural that there will be a number of suspicious smears taken from cervices ultimately diagnosed as benign. The essential in any method is a low incidence of false negative reports. As a matter of fact, in Toronto we have used Ayre's technique, immersing the spatula in Bouin's solution and imbedding the concentrate in paraffin as we think there is less chance of missing an early lesion by this method.

The question of carcinoma in situ is more debatable. Good authorities may be quoted on both sides, but for my part I feel that this condition should be kept entirely separate from early cancer where the diagnosis is based on the time-tested criterion of invasion. Otherwise, there is serious danger that in our zeal for early diagnosis we will institute an old-fashioned witch hunt resulting in needless radical treatment either surgical or radiotherapeutic. There is also the possibility of giving a false impression of the effectiveness of any method of treatment if by chance such cases should be included in an over-all survey of cancer of the cervix. I have not had any personal experience with carcinoma in situ associated with pregnancy, but I am impressed with Novak's statement that he has observed the condition to be completely reversible not only in the pregnant, but also in the nonpregnant cervix. Therefore, may I add that until invasion takes place the die is not cast nor the balance set. The fact remains that no matter how we feel with regard to the problem of carcinoma in situ, pregnancy does something to the cervix which predisposes to the development of malignant disease. Therefore, the cervix both during pregnancy and the puerperium should provide a fertile field for study by all means to determine the genesis of cancer.

We have treated 20 cases of cancer of the cervix associated with pregnancy in the last 13 years. This is an incidence of 1.7 per cent on the basis of pregnancy complicating cancer of the cervix and as 4 of the patients came from our own obstetrical department the incidence of cancer complicating pregnancy is 0.035 per cent. These figures are in line with those from other centers.

The number of cases is too small to allow anything more than some general observations. On this basis we note that 11 of the 20 patients were 30 years of age or younger. The salvage rate was lower than for nonpregnant patients and also for nonpregnant patients of a similar age group. It appears, therefore, that two factors work against the pregnant woman with cancer—pregnancy and youth.

Two of the patients developed cancer in association with first childbirth, but each of them had had a previous abortion. On the other hand 13 patients in spite of their ages, were grand multiparas having had from 4 to 10 children. This seems to indicate the importance of repeated pregnancy as an etiological factor.

The difficulties in diagnosis are indicated by the fact that the condition was not diagnosed until after childbirth in 13 patients although 7 of them had bleeding during pregnancy. In 2 cases a diagnosis of placenta previa was made and one of the patients was subjected to cesarean section, the cancer being diagnosed two months later, but in the second case the consulting obstetrician took a biopsy and made the correct diagnosis. Three other patients were examined by their attending physicians to ascertain the cause of bleeding and although biopsy was taken the diagnosis was missed. On the other hand 2 cases were correctly diagnosed although the only symptom was nonhemorrhagic vaginal discharge. I think in review that it is a reasonable assumption that vaginal smear as advocated by Dr. Hirst would have obviated some of these errors in diagnosis.

DR. WILLIS E. BROWN, Little Rock, Ark.—Carcinoma of the cervix is a serious disease with a grave prognosis. When this lesion is complicated by pregnancy the problem becomes even more grave, for the risk to both the mother and child is enhanced. It has been a privilege to have an opportunity to read Dr. Hirst's paper on "Carcinoma of the Cervix During Pregnancy" and to present this discussion. His statement, "It would seem proper at the present time to handle carcinoma in situ conservatively during pregnancy," has our wholehearted endorsement.

Carcinoma of the cervix complicated by pregnancy poses two problems, namely, the establishment of a correct diagnosis, and the application of the proper therapy. Since this paper deals largely with the matter of diagnosis rather than treatment, this discussion will deal with our experience in the problem of the diagnosis of early carcinoma of the cervix during the course of pregnancy.

Carcinoma of the cervix presents itself in two types of lesions, those which are clinically recognizable by the usual method of history and examination, and those which are preclinical in type. This latter group may be suspected from the clinical appearance of the cervix, or from the routine or selected use of smears, scrapings, sponging, etc. The review of a biopsy specimen is necessary to certify the clinical or cytological findings. The pathologist's analysis of such material usually results in one of the following four diagnoses; a normal gravid cervix, a precancerous lesion, an intraepithelial carcinoma, or a frankly invasive carcinoma. Our problem is concerned with those patients whose cervical biopsy presents a picture compatible with the diagnosis of intraepithelial carcinoma and/or a precancerous lesion.

The recognition of these states is especially difficult in the gravid cervix. The basilar hyperactivity associated with the hyperplasia and metaplasia of pregnancy is of itself at times difficult of interpretation. When these pregnancy changes are further altered by the healing of an erosion it is often extremely difficult, if not impossible, to render a final and conclusive opinion.

The case history of the young woman, aged 21, reported by Dr. Hirst is of interest. The complete regression of these atypical cervical changes during the puerperium is not unique. In February of 1949, it was my privilege to see a woman, 38 years of age, pregnant for the first time after 10 years of infertility, in whom a cervical erosion had been biopsied and reported to show intraepithelial carcinoma. In view of her age and her nulliparity, the absence of a local clinical lesion made a decision on the management of this patient most difficult. A very careful review of many biopsy specimens confirmed the diagnosis of carcinoma, possibly invasive. Fortunately, the patient disappeared from the clinic and was not seen again until she was about seven months pregnant. Examination at this time failed to reveal any clinical lesion and the biopsy showed only changes compatible with carcinoma in situ. The patient was permitted to continue through her pregnancy. She delivered vaginally without incident, and examination of the cervix at six and twelve weeks post partum failed to reveal any evidence of clinical carcinoma. Bi-

opsy, however, continued to show atypical changes. The cervix was amputated and extensive sectioning made. The findings varied from normal, through basilar hyperactivity, to areas suggestive of carcinoma in situ. Examination of this patient 9 months post partum showed no evidence of local lesion and a biopsy of the cervical stump was entirely normal.

This patient aroused our interest in this problem and random biopsies were taken on 100 normal pregnant women scattered throughout their pregnancies, the earliest at eight weeks and the latest at thirty-five weeks of gestation. This random sampling produced three additional cases in which the tissue changes were sufficiently atypical to be classified by the pathologist as carcinoma in situ, and 33 others in which there was considerable basilar hyperactivity of a confusing type.

All four of these patients were delivered vaginally without incident, and follow-up examination has failed to reveal any evidence of clinical or invasive carcinoma. Two of the patients continued to show changes compatible with intraepithelial carcinoma; in the other two these findings have disappeared.

In 1949, Dr. Novak, in a discussion of the diagnosis of carcinoma of the cervix, indicated that certain carcinoma-like pictures were found in pregnancy which were essentially indistinguishable from carcinoma and appeared to regress spontaneously following delivery. In the discussion of his paper, several others described similar experiences. Before this Society last year, Dr. Johnson presented 2 cases of caricnoma in situ during pregnancy in which the condition either disappeared following cauterization or regressed in the puerperium. Younge and his associates have reported 6 cases in which pregnancy was associated with carcinoma in situ where the reproductive function had been preserved by simple cauterization of the cervix.

The diagnosis of early (intraepithelial) carcinoma of the cervix during pregnancy is, therefore, very uncertain. Many of these very early lesions which appear malignant during the course of pregnancy apparently regress following getation. It would seem wise, therefore, to use extreme conservatism in the management of these conditions in young women. The selection of the final treatment of these patients should be determined not only by the stage of the disease as recommended by Dr. Hirst, but also by the age and reproductive wishes of the patient. In women with many children, the puerperal removal of the uterus for a suspicious, intraepithelial, or precancerous lesion would seem quite justifiable as a prophylactic procedure. However, in a young woman desiring future children the conservation of this reproductive organ and the local treatment of these equivocal lesions seems to be in order.

In conclusion, it appears that the diagnosis of carcinoma in situ during pregnancy is very difficult. Many apparently malignant changes may be reversible. Conservatism should be practiced in young women with a limited number of children.

DR. MELVIN A. ROBLEE, St. Louis, Mo.—Dr. Hirst's interesting paper and Dr. Brown's fine discussion emphasize the difficulties in making absolute diagnosis of cancer of the cervix from cervical smears and scrapings. I had an opportunity to observe these difficulties since the late Dr. Otto Schwarz of Washington University in St. Louis would request material from the Cervicitis Clinic on known benign cervical lesions in the training of those in his Cytology Department. As the personnel became more experienced, we would secure cervical scrapings from papillary erosions on women in the first trimester of pregnancy. These cells would frequently be mistaken for malignancy even by experienced observers. Biopsy and subsequent observation would demonstrate these lesions to be benign.

DR. HIRST (Closing).—I was particularly impressed by Dr. Cosbie's emphasis upon estimating the cause of bleeding in pregnancy. There is no harm in examining a pregnant patient who continues to bleed more than a week or so, and certainly from the experience of 20 cases of carcinoma in pregnancy, Dr. Cosbie has every reason for emphasizing this matter of suspected pregnancy bleeding which may very well be tumor bleeding. I agree heartily with Dr. Cosbie not to start a witch hunt. On the other hand, it seems if we

make our residents, who are largely responsible for the large amount of work in the big maternity hospitals, cancer conscious even in cases of pregnancy, we will have accomplished something, and frankly that is one of the purposes of this paper. I was very much interested in Dr. Brown's experience with 100 biopsies, many of which showed changes which were obviously pregnancy changes. In fact, his experience would indicate, or at least suggest, that our case presented from this particular series today was not carcinoma at all; but may I remind you that we have had the same technicians, the same pathologists, the same assistants, the same laboratory setup for almost four years and have examined together a great many patients, and we felt quite definitely that this patient referred to had a case of carcinoma. However, had we had confidence in this patient's follow-up we would, especially in view of a negative Gelfoam sponge smear shortly after delivery, of course, have followed this patient for a minimum of a year, if necessary doing repeated smears and biopsies rather than having been radical so early in the puerperium, but we had no confidence in her follow-up.

I was very much interested in Dr. Roblee's cervicitis clinic. I think that is a wonderful thing and certainly could be easily applied to the prenatal clinic, and I agree wholeheartedly with the proposition that the diagnosis of very early carcinoma of the cervix in pregnancy is extremely difficult.

THE MODIFICATION OF THE SCANZONI ROTATION IN THE MANAGEMENT OF PERSISTENT OCCIPITOPOSTERIOR POSITIONS*

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I T IS rather generally agreed that, at the beginning of labor in a case of normal cephalic presentation, the head usually enters the superior strait with the sagittal suture in the transverse diameter of this plane. In many instances the occiput is directed more or less posteriorly or more or less anteriorly, so that the sagittal suture does not lie exactly in the transverse diameter of the superior strait. Calkins[1] states that the percentages of these anterior and posterior deviations are approximately equal. At times the head begins its descent with the sagittal suture in an oblique diameter, usually the right oblique. It is most unusual for the head to engage with the sagittal suture in the left oblique diameter, and when it does the occiput is usually on the left side. Thus, a primary left occipitoposterior position is rare, and a primary right occipitoanterior position can be called an obstetrical curiosity.

After the early engagement of the head with the sagittal suture in the transverse diameter of the inlet, rotation of this suture into an oblique diameter (usually the right) progresses concomitant with the effacement of the cervix and the dilation of the external os, associated with descent of the head. Of course, all these developments generally proceed at a more rapid pace in the multigravida. As the occiput is on the mother's left side in about two-thirds of vertex presentations, and the right oblique is the diameter of choice, so to speak, rotation is usually anterior to the left occipitoposterior position. If the occiput is on the right side, rotation into the right occipitoanterior position is the rule. As noted above, posterior rotation at times occurs on the left side, while anterior rotation on the right side is a rarity. Many reasons for these rotations have been suggested, but we dismiss the matter simply by stating that the fetal head seems to fit the maternal pelvis best with the sagittal suture in the right oblique diameter.

It is generally held that spontaneous anterior rotation of the posteriorly directed occiput is the rule, especially if sufficient time is allowed. Danforth[2] stated that in his series of 285 private patients this occurred in 65.4 per cent. On the other hand, Dodek,[3] reporting on 514 cases at the Cleveland Maternity Hospital, encountered such rotation in only 26 per cent, and of these 133 which

rotated, 18 patients were in the second stage for three or more hours. Bill[4] agreed with Dodek on this point. Most of us feel, however (no matter what the exact percentage), that this rotation will occur sufficiently often to justify a reasonable wait. It may occur late in the first stage, early in the second stage, or late in the second stage; rapidly (as in a multigravida), or gradually (as in most primigravidas). Many teach that this rotation does not occur until the head reaches the pelvic floor, and that this is the sole causative factor. It is our opinion, however, that the change frequently begins before the head is well down on the floor, and that other factors play a part.

Frequently, no rotation occurs, giving us a persistent (or obstinate) occipitoposterior position, or the head rotates anteriorly only through 45 degrees until the sagittal suture is in the transverse diameter of the midpelvis and goes no further (deep transverse arrest). Rarely the occiput rotates posteriorly through 45 degrees into the hollow of the sacrum (occipitosacral position). The frequency of posterior positions in various clinics seems to vary considerably (Table I, from Reddoch's[5] article, apparently depending on the time at which the diagnosis is made. The percentage of failure of rotation also varies in different reports; this is probably due to the variations in the time allowed for the occurrence of spontaneous anterior rotation.

TABLE I. FREQUENCY OF OCCIPUTPOSTERIOR POSITIONS*

	VERTEX	OCCIPUTPOSTERIOR	PER CENT
Hutchinson (Tulane)	150	49	32.67
Charity	798	136	17.04
Bodek	1,785	514	29.9
Danforth	1,137	285	25.1
Lull	927	204	22.1
Scott	1,000	144	14.4

*From: Reddoch, J. W.: South M. J. 27: 615, 1934.

The management of these posterior and transverse positions varies considerably. Most obstetricians are agreed that time should be allowed after completion of the first stage for rotation to occur under the influence of the labor pains. The length of this period varies in different clinics, and in different patients in the same clinic. A wait of 1½ to 2 hours in the second stage is the time usually set for this expectant period. As a matter of fact, many competent obstetricians do not wait this long, feeling that early expert correction is perfectly safe, even though they admit that many of these heads probably would have rotated spontaneously, had they waited longer. In many instances, a wait much longer than 2 hours is safe and proper, especially if the attendant is not skilled in rotation of the fetal head.

It requires much judgment (acquired through experience) to decide when the point has been reached after which a further wait is inadvisable. The usual signs of maternal and fetal distress are taken into consideration. In addition, we must mention two important points. One is that serious intracranial damage may develop before any signs are discernible. Such a condition may be suspected if the uterine contractions are strong and frequent and rotation is not resulting. The second point is that prolonged hard labor pains might produce so much

molding of the fetal head that anterior rotation, manually or with forceps, be-
comes difficult or impossible, and internal podalic version in particular is very
hazardous. In some patients, indication for interference may arise before the
cervix is completely dilated; here the employment of Dührssen's incisions, if the
proper conditions are present, is a most useful preliminary procedure.

Many methods are suggested for the management of this condition, each
obstetrician choosing the one in which he is most skilled. Digital pressure on the
posterior parietal bone during the pains, pressing this region upward and for-
ward, will frequently coax the head around. Having the patient lie on the side
toward which the occiput points, in Sims' position, will at times be sufficient.
Manual rotation is the choice of many. Danforth[2] stated that he employed it
routinely, and that he used it in 76 out of 98 cases (in his series of 285) in
which spontaneous rotation did not occur. This maneuver will suffice in most
instances, but is rather difficult if the head is impacted and molded; those ex-
pert in its performances can usually overcome these difficulties. Internal podalic
version and breech extraction are favored by many. If performed early, as
was done by Bill[4] in 317 out of 500 cases, the risks are slight and the results
are satisfactory if the operator is skilled and the proper conditions are present.
Late in the second stage the procedure is difficult and the danger of uterine
rupture is considerable. Beacham[6] has reported 10 out of 96 cases of rupture
thus produced. To Pomeroy is ascribed the manual rotation of the anterior
shoulder by the hand introduced internally well up into the uterus. DeLee[8]
advocated manual rotation, or the so-called key and lock method; this consists
of a gentle application of the forceps obliquely to the head, with a 10 degree
rotation, reapplication, and a continuance of this maneuver until the occiput
is under the symphysis. Many prefer the Kielland forceps, others the Barton
instrument.

In our hands, forceps rotation by a modification of the Scanzoni method has
been the procedure of choice for many years. In order to know just what
Scanzoni advocated, Reddoch[5] and I translated his description of the procedure.[3]
I quote this translation from Reddoch's article:

"The head stands with the forehead turned toward the front and left, so that the
sagittal suture passes in the right oblique diameter; the left blade is applied in front of the
left sacroiliac synchrondrosis, the right behind the right obturator foramen; with this the
transverse diameter of the forceps is placed in the left oblique diameter of the pelvis, their
concave edges and tips are turned to the anterior circumference of the left lateral hemisphere
of the pelvis, and so also with the forehead. An eighth of a circle is now described with
the instrument, directed from left to right, whereby its right blade comes to rest under the
symphysis, and the left in the hollow of the sacrum; and in this way, the head is rotated,
the earlier standing forehead is moved to the middle of the left lateral wall of the pelvis
and the sagittal suture is placed parallel with the transverse diameter of the pelvis.

"Now both blades of the forceps are removed, and again applied, so that the left blade
comes to lie behind the left obturator foramen, the right in front of the right sacroiliac liga-
ment, whereupon by the next rotation the occiput is brought completely under the pubic arch."

As will be seen, Scanzoni rotated the head from occipitoposterior to occi-
pitotransverse, then reapplied the forceps. Williams,[9] in his text, and East-
man,[10] in his revision of this text, advocate rotation through 90 degrees to occi-

pitoanterior. Long before we read Scanzoni's description, we had been practicing rotation of the occiput through 135 degrees, until it lay under the symphysis pubis, and we still employ this method. It is very similar to Bill's technique, used by him 172 times in his series of 500 cases. Just how many hundred times we have used it in private practice, in our teaching service at Charity Hospital, and in consultation, I cannot say, as it would be necessary to go through thousands of records to obtain the figures. A review of 1,000 unselected records of private obstetrical cases shows that this rotation was performed in 97 of these patients, without maternal or fetal mortality.

Many writers have stated that rotation by the Scanzoni method or its modifications may cause deep lacerations of the vagina, may cause serious injury of the bladder, or may produce some avulsion of the bladder supports with consequent cystocele. Our answer is that we have never experienced such complications, and that the end results, as noted on subsequent examinations, have been very satisfactory. Of course, one or more deliveries of large babies by any method (spontaneous, forceps, breech, version), may be followed by vaginal relaxation, cystocele, and rectocele, because of the stretching of the subjacent tissues incident to the passage of large infants. But we have seen no serious soft-tissue damage ascribable solely to forceps rotation.

I shall review briefly the technique of the method, including a step recently adapted by us to prevent the rotation of the head back toward its original position, and to facilitate the shifting of the second blade, as for some reason we found that at times it was rather difficult to remove it completely from the vagina. In a right occipitoposterior position, the right hand is introduced posteriorly and to the left, with the fingers inside the cervical rim, if it has not completely retracted out of the way. The left blade of forceps is introduced along the hand, and is fitted over the left parietal bone, which is posterior. It is held by an assistant. The left hand is then introduced in the right side of the vagina anteriorly, over the anterior parietal bone (inside the cervical rim, if present), and the right blade is guided into place over the anterior (left) parietal bone. The forceps' blades are now locked, the curve that is ordinarily directed toward the occipit being toward the child's face. If deflexion is present, it is now corrected by manipulating the forceps. The head is now disengaged, if necessary, by lifting it up in the vagina with the forceps. It is now rotated clockwise, either by swinging the handles around or by simply rotating the instrument; this is continued until the occiput is swung around to lie directly under the symphysis; no traction is made during this rotation. The maneuver is aided by an assistant, who rotates the anterior shoulder from right to left by abdominal manipulation. The position of the occiput is checked by vaginal examination, and when it is in the proper position, it is fixed as well as possible by a little downward traction. The blades are, of course, upside down, and must be reversed. The blade in the right side of the vagina, over the baby's right parietal bone, is entirely removed by carrying the handle down toward the mother's perineum. The blade in the left side of the vagina is loosened by manipulation, and guided by the fingers is swept around the posterior vaginal wall from left to right, past the baby's face. This is facilitated by swinging its handle in the opposite direction by the external hand. This blade is now right side up in the right side of the vagina, over the baby's right parietal bone. The other blade is now introduced right side up in the left side of the vagina, over the left parietal bone. It is now necessary to swing the handle of the
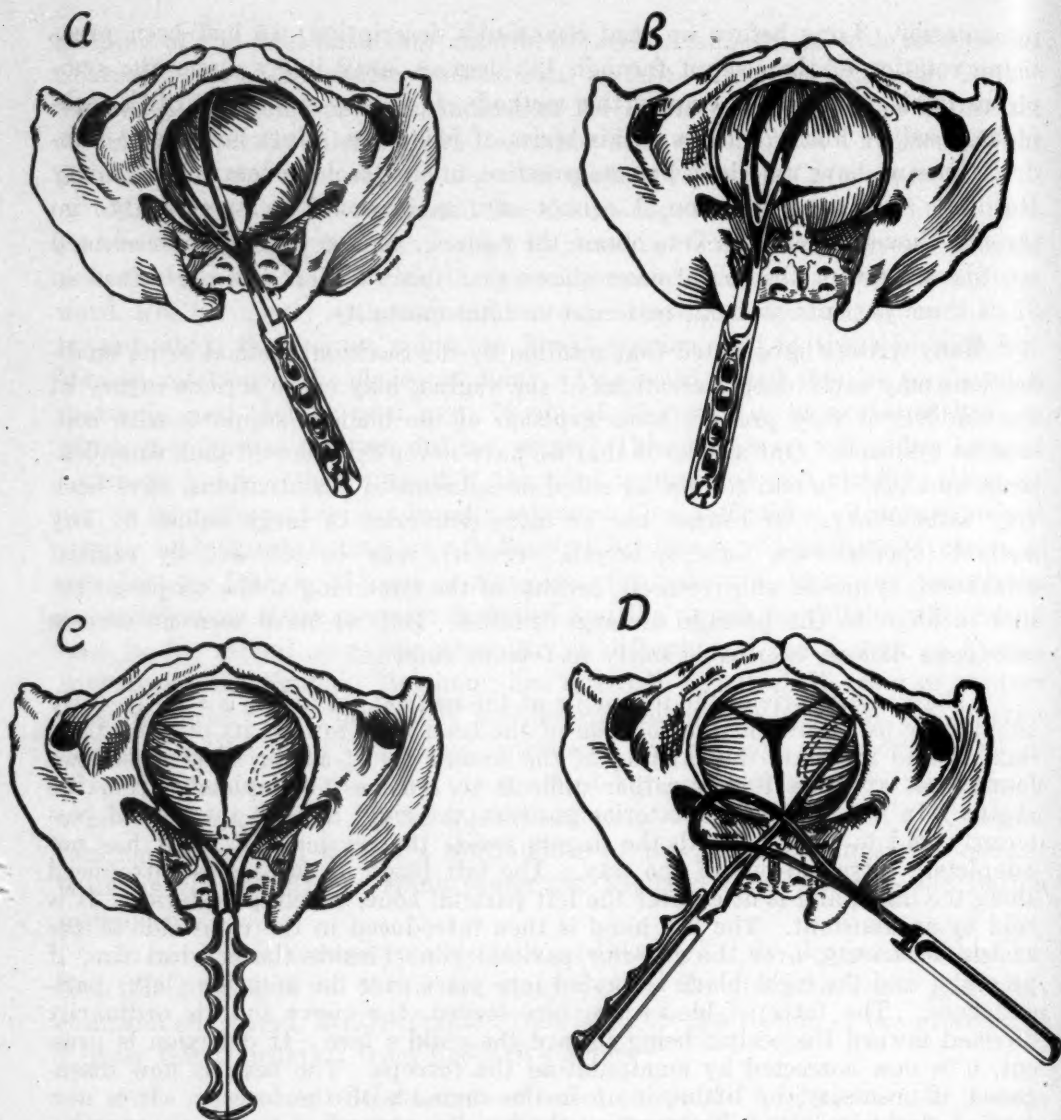
Fig. 1.—*A*, First position of forceps. *B*, Rotation to right occipitotransverse. *C*, Complete rotation to occipitoanterior. *D*, Removal of right blade of forceps. *E*, Beginning rotation of left blade. *F*, Completion of rotation of left blade. It is now looking toward occiput. *G*, Introduction of second blade. *H*, Locking of blades.

second blade around and below the handle of the first (right) blade in order to lock them. Delivery is now effected, a left mediolateral episiotomy being performed when the head is well down on the perineum. As stated above, this manipulation of the left blade, for some reason, is frequently easier than its complete removal, which we practiced formerly. We feel that this maneuver often prevents the rotation of the head back to its original position, which happens occasionally when both blades are removed. In a few instances, this backward rotation occurs in spite of the rapid shift of the second blade. Then it is necessary to start over and rotate the head again. Now a second pair of forceps is employed, using Seides'[11] method. The right blade of the first pair (upside down) is removed, and the first blade of the second pair is inserted
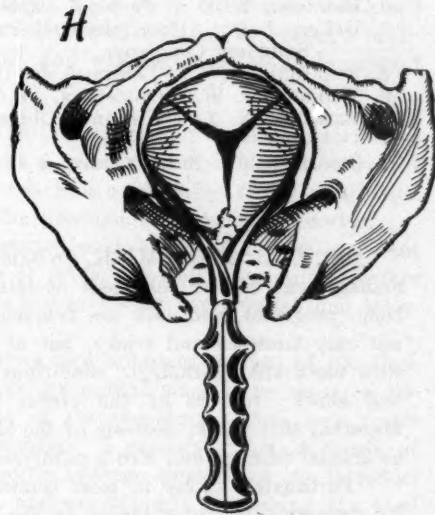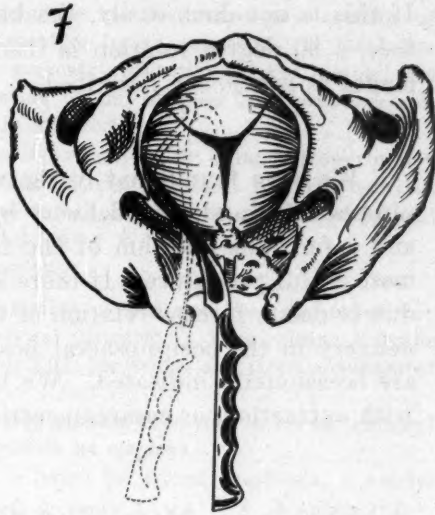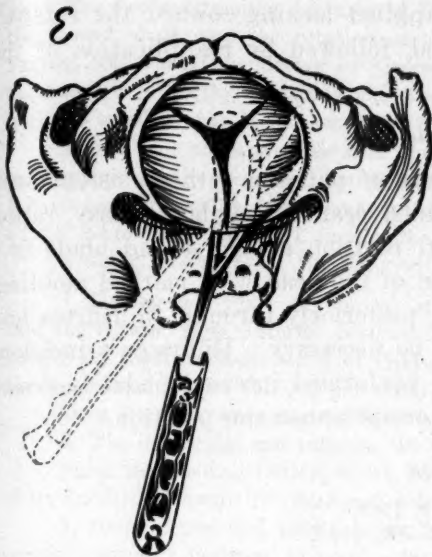
to the right of the head, right side up, while the second blade of the first pair, being still in place, holds the head in position. Then the second blade of the first pair is removed, the second blade of the second pair is introduced, and delivery is accomplished.

In dealing with a case of deep transverse arrest, it is frequently possible to rotate the occiput anteriorly manually; or, one blade of the forceps applied over the posterior parietal bone (reminiscent of the old vectis) may lever the occiput forward, especially during a uterine contraction, or, one might be able to introduce the forceps over the parietal bones, looking toward the occiput, the anterior blade being introduced behind the symphysis, the posterior one in the hollow of the sacrum (as in the reapplication originally described by Scanzoni).

If this is not done easily, the blades are applied looking toward the infant's face, a 90 degree rotation is then performed, followed by reapplication of the blades as previously described.

Conclusions

We have found that in the vast majority of patients with persistent occipitoposterior positions, delivery by the modified Scanzoni method is easy, rapid, and safe. The addition of the intravaginal rotation of the second blade is a most useful procedure. If there is impaction of the head with marked molding, due to delay, forceps rotation of the occiput posteriorly through 45 degrees and delivery in the occipitosacral position may be necessary. Dührssen's incisions are occasionally indicated. We have never performed internal podalic version with extraction, or cesarean section, for an occipitoposterior position.

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Discussion

DR. C. O. McCORMICK, Indianapolis, Ind.—For the average obstetrical attendant the management of the persistent occipitoposterior position continues to be a *bête noir*. His time, judgment, and skill are frequently taxed, and from his point of view the situation is not only tiresome and tricky, but at times treacherous. He is aware of the possibility of such associated pathologic conditions as uterine inertia; maternal exhaustion, hemorrhage and shock; rupture of the uterus from internal version; severe forceps trauma to the maternal soft parts; necrosis of the bladder wall; and likewise such gross injuries to the baby as cranial damage and Erb's paralysis.

Fortunately today in most communities and clinics such cases are either voluntarily or by departmental rules placed in the hands of expert obstetricians with the result that the maternal and infant damages are but little increased over those of normal occiput anterior positions. That the modified Scanzoni operation applied expertly can play an important role in this achievement is well shown in Dr. King's presentation. A series of 97 unselected cases handled successfully in a series of 1,000 deliveries is more than casually convincing. Dr. King attributes this success in part to a modification of the Scanzoni technique, which he and his staff have developed.

The three major modifications, that of Tarnier, the wide circumduction of the handles; that of Bill, secured flexion of the head; and now this one, the intravaginal rotation of the second blade, so lucidly demonstrated by the essayist, go far in stressing the fundamental value of the Scanzoni principle.

Although the employment of the Scanzoni operation has been discounted, having been described as ''entirely dispensable'' and ''fraught with too great dangers,'' it would appear, when employed with modifications, at least by experts, it is an easy and safe method of handling obstinate posteriors, and is worthy of more routine usage.

The two outstanding features of Dr. King's technique are the intravaginal rotation of the second blade, and the rotation of the anterior shoulder by an assistant. If the intravaginal rotation or wandering of the second blade prevents restitution of the occiput, the maneuver is a worthy contribution. The direct rotation of the shoulder is a practical aid, and one wonders why it has not been more commonly adopted.

I have had no experience with the modification described by Dr. King. However, my employment of the Scanzoni delivery has always been satisfactory, and like the essayist, I have been spared by fortune any gross maternal or infant injuries. Occasionally, instead of the Scanzoni technique, I employ the single application of Williamson.

I would like to favor Dr. King with a few questions:

1. During my years of clinical and private practice, it has not been my experience that the occiput right anterior position is an ''obstetrical curiosity.'' This opinion is borne out by the roentgenologic study of Caldwell and Moloy (6.5 per cent), and later corroborated by Steele and Javert (5.7-9.6 per cent).

Does Dr. King have any explanation as to why this position is so rare in his community?

2. The doctor did not refer to the type of anesthesia he employs.

Since the medical center, which he represents, is noted for spinal anesthesia, I wonder if he finds it adequate for Scanzoni delivery.

3. Since contracted pelvis is an important etiological factor in producing persistent occiput posterior position, to what extent does he employ radiographic study of the pelvis?

4. From his statement that he has never performed internal podalic version with extraction in handling occipitoposterior positions, are we to infer he is adverse to doing so?

It is my impression those of us who serve parturient women will find Dr. King's modification of the Scanzoni operation a very helpful aid, and will accept it as an important contribution.

DR. J. BAY JACOBS, Washington, D. C.—As to the etiology of occipitoposterior, as already mentioned, I believe that we are concerned to a great extent with the contour of the pelvic inlet since the process is one of adaptation as well as possibly faulty inclination of the inlet. I think that faulty inclination favors the production of occipitoposterior.

As to the incidence of this condition, there is reported a variation of 4 to 40 per cent depending upon the time in labor when the diagnosis is made. Obstetricians who interfere early would encounter higher incidence than those who are extremely conservative and interfere late.

The method of treatment varies. Some conservative men advocate the use of the Beck binder. Some use the Pomeroy maneuver, which I consider radical since it necessitates disengagement of the head and internal manual rotation of the shoulders. Some men resort to version and extraction, which also is radical treatment. I personally am in favor of forceps rotation because I do not think the average pelvis is large enough for the introduction of the hand without disengagement of the head, and am opposed to pushing the head up or disengaging it. Forceps rotation can be done quite simply, and I do not think it necessary to rotate the shoulders in performing the Scanzoni manuever. The head may be rotated 225 degrees on its vertical axis without any risk to the fetus, and usually without trauma to the mother, provided, of course, the rotation is performed without making traction at the same time. I have never rotated a forceps blade inside the pelvis as Dr. King describes, but I can see that there may be some advantage to it. As a rule, firm pressure upon the fundus by an assistant prevents backward rotation of the head during the process of reapplication of forceps.

As you know, I have designed a pair of forceps intended for the treatment of persistent occipitoposterior. The main feature of this instrument is the incorporation of a joint between the blades and shanks, with a button in each handle which permits alteration of the pelvic curve. With this instrument, one may perform the Scanzoni maneuver with a single application. For instance, when treating a right occipitoposterior one would apply the forceps as for a left occipitoanterior. With moderate traction, the head is brought into mid-pelvis, the pelvic curve is made to disappear, so that the handles may be turned as one would a

screwdriver, thus bringing the occiput to the anterior position. By pushing the buttons a
second time, the pelvic curve again appears and the head is extracted as with classical for-
ceps. The advantages of this procedure are that the forceps are easily applied as for a
left occipitoanterior, rotation and extraction are readily completed without describing a
large arc inside the pelvis and without the forceps being improperly applied. Thus, trauma
to the mother is avoided and rupture of the falx cerebri and tentorium cerebelli, which
results from oblique application of forceps to the fetal skull, is also avoided.

DR. S. A. COSGROVE, Jersey City, N. J.—We are not discussing the management of
occiput posterior positions. Dr. King's presentation is specifically about a technique of
forceps application by the Scanzoni principle. He has made a very ingenious modification
of that principle. It occurs to me that there is an even simpler modification which I used
many years ago. That is to apply the forceps initially upside down in relation to the pelvis.
You now have the head in the forceps with proper cranial prehension. The situation, as you
apply the forceps, is exactly the same as at the finish of rotation where you have made your
forceps application primarily in proper pelvic relationship but with poor fetal prehension.
Therefore, this technique presents no difficulty that any other technique of forceps rotation
with the classical type of forceps represents. Then, having made your rotation, the forceps
are now in proper pelvic relationship and in proper fetal relationship. There is no necessity
for removing and reapplying them, and the extraction can be immediately performed.

DR. KING (Closing).—As Dr. Cosgrove said, we did not try to go into details regard-
ing the various methods of delivering occiput posterior position. Those who prefer internal
podalic version and are skilled at it employ it. I have not delivered any infants in pos-
terior occiput presentation by internal podalic version. I started off a number of years
ago with the Scanzoni method, and have continued to use it. As I see it, if you do the
version early, all right; if you wait until rather late and the water drains off and the
head becomes impacted then the version is more dangerous.

Dr. McCormick has asked whether occiput posterior is rare or not. In my opinion,
early in the first stage I find this position common.

In this method a general anesthetic is used. We found that one thing we should not
do is to use a saddle block in occiput posterior, even though it originated in New Orleans;
we do not use it until the head is well down. We study roentgenologically practically all
primigravidas and if a contracted pelvis is found, of course, that is another story. In that
case the procedure would have to be individualized.

Dr. Jacobs' special forceps are satisfactory. Someone mentioned that we might use the
Kjelland forceps. It is well fitted for this purpose, but I am not in the habit of using it.

About Dr. Cosgrove's idea, I have tried it sometimes but somehow or another I am
not adept at it. I have found it difficult to apply the forceps upside down and I just could
not make it work. I have always preferred the original method as described above.

PREGNANCY FOLLOWING NEPHRECTOMY*

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WITH improvements in surgical techniques and the broadening of medical indications, the operation of nephrectomy is becoming less uncommon. The indications today include many diseases and conditions which occur during or even prior to the childbearing years, so that pregnancy following nephrectomy is now seen more often. However, these occurrences are infrequent enough to render it impossible to arrive at an accurate incidence of pregnancy associated with a lone kidney and no one physician sees a sufficiently large number of cases to supply figures of absolute statistical value.

Apparently, the first case of pregnancy after nephrectomy was reported by Schramm[1] in 1896. During the past forty years, numerous case reports have appeared in the literature as well as larger and collective series by Hartmann,[2] Pousson,[3] Matthews,[4] and Prather and Crabtree.[5] Obviously, many cases have not found their way into the literature during more recent years because of the loss of the novelty nature of the occurrence. Originally, it was considered unsafe for a patient to undertake pregnancy after nephrectomy and these patients were advised against subsequent pregnancy and even against marriage. Such advice was not always heeded and it was found to be safe, at least under certain circumstances, to carry a pregnancy normally with but one supporting kidney. Ultimately, nephrectomy during pregnancy was undertaken and presented problems which were not unsurmountable. As early as 1894, Israel[6] accomplished a nephrectomy for tuberculosis in the fourth month without upsetting the pregnancy. By 1913, Hartmann[7] was able to report a series of thirty cases of nephrectomy done during pregnancy. Mussey and Crane[8] added nine cases and recommended nephrectomy during pregnancy if required for the life and health of the patient. Nephrectomy done at this time produces essentially the same end results as when done in the nonpregnant state and with little increase in mortality.

There is fairly uniform agreement that generally the patient with a lone kidney can carry a pregnancy without undue fear that the remaining kidney will be damaged by the experience. There must, however, be careful selection of the patients permitted to proceed with childbearing. For example, patients with nephrectomy for malignancy should perhaps never be allowed subsequent pregnancy since these tumors are so frequently recurrent, and those with congenital cystic disease should not be sanctioned as mothers because the disease is a bilateral one. Again, renal tuberculosis is one of the most serious of the renal complications. Some feel so strongly against pregnancy following nephrectomy for tuberculosis that they advise surgical sterilization while

others will allow it if a period of two to four years elapses without evidence of reactivation of the tuberculous process in any other part of the body. A damaged lone kidney from either vascular or infectious processes is a definite contraindication to pregnancy. Also, the risk of complications in pregnancy is greater when the right kidney is the remaining one, for lone upper urinary tracts undergo pregnancy changes similar to those seen when both kidneys are present, and the right is more subject to ureteropelvic dilatation, urinary statis, and infection.

In the kidneys, as in many other organs, there is a large "factor of safety" and it has been estimated that we normally have from three to six times the amount of renal tissue required to meet our needs. Therefore, even if one kidney be lost without any compensation on the part of the remaining one, the patient would not be particularly inconvenienced, provided the remaining kidney be a healthy one. But it has been shown repeatedly that within three to four weeks the normal remaining kidney does undergo compensatory hypertrophy and does take over the function of both kidneys, leaving the patient with approximately the same life expectancy as that of a person with two normal kidneys. Welsh, Wellen, and Taylor[9] have demonstrated that these conversion changes are not affected by pregnancy when nephrectomy is performed during the course of a gestation.

It is agreed that pregnancy increases the work to be performed by the kidneys and that this extra burden becomes heavier with the advancement of the pregnancy. The question then which should be answered for every patient contemplating pregnancy with a lone kidney is whether that remaining kidney should be subjected to the additional work. The quantitative nature of the "strain of pregnancy" on renal tissue has never been defined as it has been for the heart. But, in spite of the absence of such specific data, great care must be taken to prove the lone kidney normal before sanctioning conception or before allowing a pregnancy to proceed. Moreover, the course of such pregnancy must receive additional study in order to detect the earliest possible evidence of risk to the last storehouse of renal tissue, for most observers are of the opinion that pregnancy should be terminated upon the development of either toxemia or upper urinary tract infection. It is not sufficient to see the patient with the usual frequency and to perform the routine prenatal procedures. Considerable reduction of the renal functional reserve may occur without conspicuous symptoms. It is the frequent silence of this depreciation which makes it necessary to apply particular tests to reveal and/or measure the status of the renal functional capacity. To wait until some of the most conspicuous signs or symptoms develop is reprehensible procrastination. The absence of proteinuria, edema, or hypertension does not prove that the renal function is normal.

Prather and Crabtree[5] rightfully insist upon routine prenatal urinalyses being done on catheter specimens from patients with a single kidney. They consider this far more important than the risk of introduction of infection

through careful catheterization. To this must be added several urine cultures arbitrarily spaced during pregnancy and the puerperium or more often if suggested from routine analyses.

Unfortunately there is no single renal function test which has been universally acceptable to all clinicians or investigators. Many have been devised but each has some shortcomings. A most careful clinical study of several of these was made by McGee and Martin.[10] They applied several tests to each of 290 patients in whom renal disease was suspected from history and physical examination. In only one-third of the cases did all tests confirm renal impairment. Their fractional P.S.P. test gave expected results more often than any other measure employed, failing to do so in 19 per cent of the cases, while the urea clearance test failed in 32 per cent, and the dilution-concentration test in 40 per cent. When combined with urea clearance, the 15-minute P.S.P. test produced laboratory confirmation of renal disease in all but 2 per cent of the patients presenting good clinical or urinary sediment signs of renal disease. They concluded that their modification of the P.S.P. test could not be displaced by any available procedure from point of view of convenience and accuracy for clinical use. This has been our own experience and we have not routinely applied other tests in the study of renal function in cases of pregnancy following nephrectomy.

The many advantages of the P.S.P. test claimed by Rowntree and Geraghty[11] in 1910 are accepted. These make it the best adapted of all drugs thus far for functional renal tests. The test will furnish all information possible from any other one and will supply it more quickly and with more accuracy and precision so far as the physician is concerned and with no injury or discomfort to the patient. The only disadvantage to its use in the cases under consideration occurs in the advanced pregnancy when urinary statis in the upper tract may unduly prolong the appearance time and thus cause a corresponding shift to the right in the peak time of excretion.

The original two-hour P.S.P. test was not found to be as sensitive as desired to demonstrate minor changes in renal function. This disadvantage has been overcome since Shaw[12] instituted intravenous instead of subcutaneous injection of the dye and collection of urine samples at 15-minute instead of hourly intervals. It is this modification of the test which we have employed in the cases of lone kidney. Considerable importance is attached to appearance time and the normal range of this is three to five minutes. We place the patient in Fowler's position and utilize an indwelling catheter so placed that urine entering the bladder will immediately drain through the catheter into a collection basin. Only in this way is it possible to obtain prompt appearance times and accurate 15-minute specimens.

Rowntree,[11] Shaw,[12] and others proved that the elimination of phenolsulphonphthalein was independent of the fluid output in normal patients. Snowden,[13] however, showed that in severe cases of nephritis there is difficulty in concentrating the drug and that the elimination of 'phthalein is materially increased in these cases when the urinary flow is stimulated by forcing fluids, i.e., in chronic nephritis the process of excretion of phenolsulphonphthalein

becomes one of simple filtration. It is this fact which led us to force fluids for one hour prior to and for the first hour after the injection of the dye, to consider any specimen as inadequate unless it contained at least 100 c.c. of urine, and to measure the urinary output for 15 minutes immediately prior to the start of the test. An added feature in forcing fluids is that the dye should thus be more completely washed down the urinary tract. Shaw[12] considers samples with as little as 50 c.c. of urine as ample for a satisfactory test.
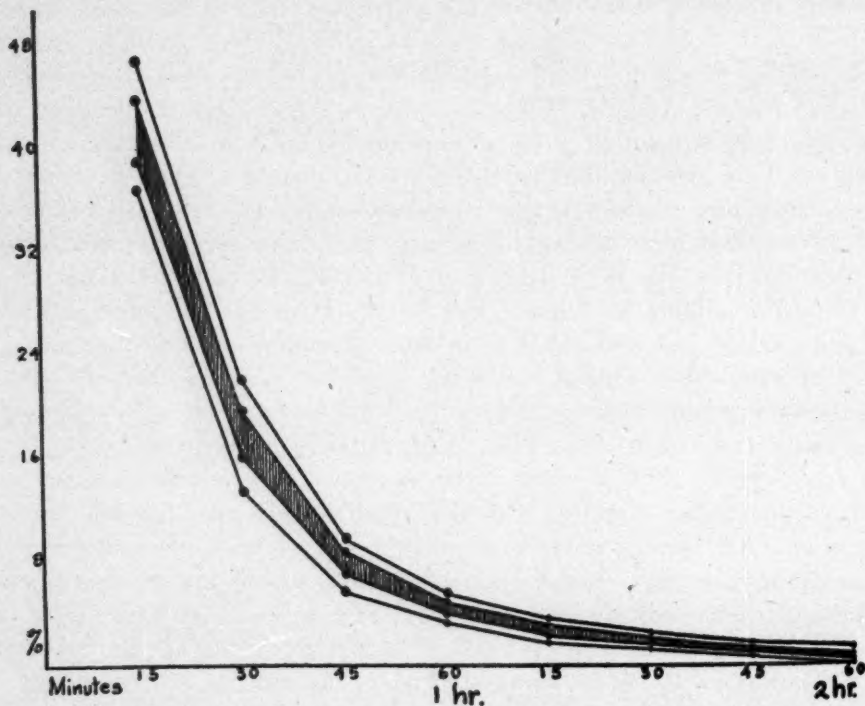
Fig. 1.—Curve of elimination of phenolsulphonphthalein in normal cases (Shaw).

Fig. 1 is reproduced from Shaw's[12] original work to show the curves of elimination of phenolsulphonphthalein as determined from 23 cases considered normal. Here it is seen that the peak of excretion occurs in the first 15 minutes after intravenous injection of the dye and this amount approximates the total dye for the remaining periods. Also the amount of dye in each succeeding specimen is approximately one-half of that in the preceding period. Chapman[14] and others rather arbitrarily consider 25 per cent excretion of the dye in the first 15-minute interval as the lower limit of normal.

The earliest departure from normal renal efficiency is indicated by an increase in the appearance time and by a decrease in dye elimination in the first 15-minute specimen with a corresponding increase in the later specimens. A typical curve of this kind was produced with Case 3 (Fig. 4). As renal failure advances, the peak of elimination shifts farther to the right and the curve tends to flatten out. It is particularly significant that an abnormal elimination of the dye is reflected chiefly in the first period, making this specimen by far the most important. If it contains at least 25 per cent of the dye, it alone

would be sufficient for practical purposes. But like other clinical tests of organ function, a single fractional P.S.P. test must not be accepted as proof of impaired renal function unless it fits the clinical picture.

The following case reports are not intended to swell the number of reported cases of pregnancy following nephrectomy but are selected ones representing types encountered during the past seven years.

CASE 1.—J. S. This patient was an unregistered, white, private 27-year-old, para 1-0-0-1, whose last menstrual period had begun eight weeks before she was first seen.

She had had the usual childhood diseases without known complications. There had been an automobile accident nine years ago with mild cerebral concussion, a fracture of the back and neck, from all of which she had recovered without obvious permanent injury. She had had hemorrhoidectomy and an unspecified operation of the uterine cervix five years ago.

Her health is said to have been good until six years ago when she developed bilateral kidney infection at about six weeks' gestation. She was treated medically throughout the pregnancy with questionably good control of the infection. Late in pregnancy, there was a severe and acute flare-up of the pyelitis characterized by chills and high fever. The delivery was at term, with the production of a 7 pound, 11 ounce living child. A year later, because of what is said to have been a "severe kidney infection resulting in destruction of the right kidney," a nephrectomy had been done. Since that time she had had almost constant low back pain, dull in character on the left side, occasionally radiating into the corresponding flank area, with intermittent episodes of urinary frequency and dysuria, and occasionally associated with hesitancy. The last such episode occurred one month before her last menstrual period. She had had no therapy and no renal function tests since nephrectomy. She was told not to undertake another pregnancy but no contraceptive advice was given.

Physical examination revealed a small statured, slenderly built young matron, in apparent fair health. The old (right) nephrectomy scar was obvious. There was mild tenderness in the left costovertebral angle and along the course of the corresponding ureter. There were no abdominal organs palpable. Pelvic examination showed a uterine corpus corresponding in size to the period of amenorrhea. There was a low-grade fever and the catheter specimen of urine contained a moderate number of pus cells in clumps. Blood studies were within normal limits. Fractional P.S.P. test produced normal readings (Fig. 2).

The following observations were made at cystoscopy: scarring of the bladder neck with annular contracture; hyperemia of the urethra; small polyps in the bladder neck; atrophy of the right ureteral orifice; trabeculations in the lateral quadrants of the bladder; slight diminution of bladder capacity; difficulty in passing a No. 4 olive-tip catheter through the left ureteral orifice up to the renal pelvis; a moderate amount of residual urine in the left kidney pelvis containing few epithelial cells and occasional pus cells; and intravenous indigo carmine appeared in good concentration within 2½ minutes. Retrograde pyelography showed: no evidence of pyelonephritis; some tortuosity of the ureter; good drainage in the upright position; and no appreciable nephroptosis.

The consulting urologist was of the opinion that this amount of urinary tract abnormality and infection in a lone kidney should not be complicated by a current or future pregnancy. Consistent treatment for clearance of the vesicle neck obstruction was to be followed by prophylactic dilatations of the ureter as imperative to protect future renal function and prevent infection and stone formation.

Under intravenous Pentothal Sodium and curare anesthesia, an abdominal subtotal hysterectomy on the unopened uterus was performed as the method of choice in effecting therapeutic abortion and sterilization. The postoperative course was smooth and uneventful with the patient leaving the hospital and the state on the sixth day. Follow-up studies and information are not available.

In this case, it was seen that the lone (left) kidney presented very good function. From this point of view, she would have been an acceptable subject for pregnancy. The already present infection, on the other hand, in addition to the serious scarring and obstructive pathology made continuation of this or the undertaking of a subsequent pregnancy an extremely hazardous experience as regards preservation of normal renal tissue.
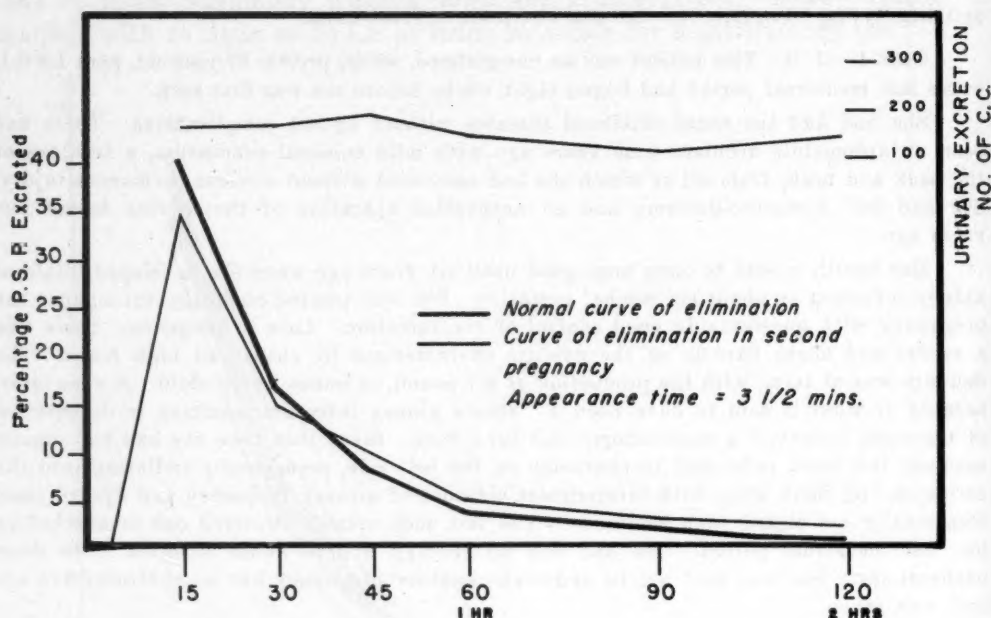

Fig. 2 (Case 1).—Patient J. S. Curve of P.S.P. elimination in a 27-year-old secundigravida with infection of the remaining left kidney and serious obstruction of the lower urinary tract.

CASE 2.—J. D. O. This patient is now a 26-year old, white, para 2-0-0-2, with normal pelvis, negative serology, and Rh positive. Her younger child is four months old at this time.

The family history is important only because the maternal grandmother died of angina at the age of 57 years. The patient herself had had the usual childhood diseases without known complications. However, she had also had pyelitis in childhood and tonsillectomy and adenoidectomy at the age of 7 years. Of paramount interest is the fact that when 20 years old, during her student nurse's training, she had left nephrostomy performed in connection with removal of a large staghorn calculus and nephrectomy five months later. Intravenous pyelography had revealed that the remaining (right) kidney was normal with normal excretion of the dye. No other renal function tests had been done at any time.

She was first seen when the initial pregnancy had advanced through 14 weeks. General physical examination showed a medium-statured young primigravida in apparent good health. Fractional P.S.P. test produced a normal curve of excretion. Catheter specimen of urine contained no formed elements and grew no bacteria on several different media. The pregnancy proceeded normally with maximum blood pressure readings reaching 146 systolic and 78 diastolic. Urine remained free of protein throughout, there was no edema, and no other evidence of pregnancy toxemia appeared. Three weeks prior to her estimated date of confinement, the membranes ruptured spontaneously and prematurely and labor began promptly thereafter. The labor lasted only 3½ hours with termination by elective low forceps extraction under intravenous pentothal sodium anesthesia, a 6 pound, 11½ ounce normal and living male child being obtained. The puerperium was normal and

uneventful. Five days after delivery, as during the last trimester, renal function tests and urine cultures were repeated and found to be essentially the same as the original tests. The later puerperal follow-up showed no evidence of toxemia or of renal impairment. Contraceptive advice was given. Complete urological studies three months after delivery produced normal upper urinary tract findings with no retained pregnancy effects.
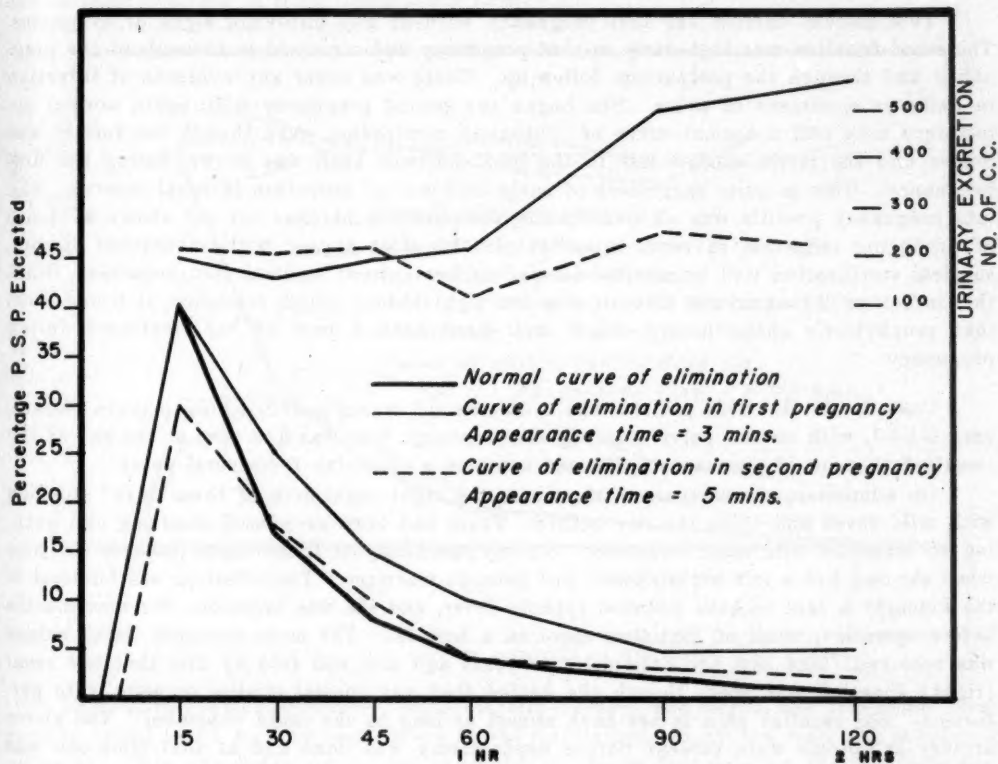

Fig. 3 (Case 2).—Patient J. D. O. Curves of P.S.P. elimination in a 26-year-old para 2-0-0-2 with a normal lone right kidney. Pyelitis developed late in the second pregnancy.

Approximately three years later, she returned at the end of the second lunar month in her second pregnancy. General physical examination revealed no pathologic conditions. The pregnancy appeared normal. Blood picture and urine findings were not abnormal. Fractional P.S.P. test at this time produced a normal curve but the maximum excretion, as is seen in Fig. 3, was not as high as with the previous pregnancy. The urine contained no protein or formed elements and no bacteria were grown from it. Similar tests were repeated and like results obtained in the last trimester and seven weeks after delivery. The pregnancy progressed normally with maximum blood pressure of 138 systolic and 74 diastolic, and a total weight gain of 23 pounds. A mild hypochromic anemia which appeared early in the last trimester rapidly responded to iron therapy. However, three weeks before her estimated date of confinement she complained of generalized malaise for about a week and reported having had a chill the day before, followed by fever to 101.2° F. She had immediately begun forcing fluids and taking of a sulfonamide, feeling better upon reporting for a prenatal visit. There was some bladder tenderness but no costovertebral or renal (right) pain or tenderness. Catheter specimen of urine presented many pus cells, some of these in clumps, with a few red blood cells and epithelial cells but little proteinuria. She was immediately hospitalized and labor was promptly induced by artificial rupture of membranes. She had a rather short latent period and short labor with elective low forceps delivery under saddle-block anesthesia, a normal, living, 7 pound, 1 ounce male

infant being delivered in good condition. Urine cultures, the first of which was obtained approximately 24 hours after the exhibition of chemotherapy, failed to grow any organisms. She had no fever after the initial chill, therapy was continued throughout her hospital stay of one week and formed elements disappeared from the catheterized urine before her discharge. Check-up examination at seven weeks following delivery was normal throughout. She has not yet had her final and complete urological check.

This patient carried her first pregnancy without any untoward signs or symptoms. The renal function was high early in that pregnancy and remained so throughout the pregnancy and through the postpartum follow-up. There was never any evidence of infection in catheter specimens of urine. She began the second pregnancy with again normal appearance time and a normal curve of 'phthalein elimination, even though the former was longer and the latter cleared less in the first specimen than was shown during the first pregnancy. This is quite suggestive of early evidence of reduction in renal reserve. The late pregnancy pyelitis was an unfortunate complication but has not yet shown evidence of producing reduction in renal capacity. If this does appear with subsequent studies, surgical sterilization will be advised instead of her current medical contraception. Since this infection did occur and since it was her right kidney which remained, it would seem that prophylactic chemotherapy might well have been a part of her treatment during pregnancy.

CASE 3.—L. H. This patient was a 34-year-old, unregistered, white, private patient, para 0-1-0-1, with normal pelvis and negative serology, who was first seen at the end of the twenty-first week of pregnancy. She had not seen a physician for several years.

On admission, she compained of pain in the right renal area of three days' duration with mild fever and chills the day before. There had been associated smarting and burning on urination with some freqeuncy. Strictly speaking, her illness dated back to the time when she had had a left nephrectomy, just prior to marriage. The infection was bilateral in the kidneys, is said to have followed typhoid fever, and she was bedridden for nine months before operation, much of that time spent in a hospital. The more damaged (left) kidney was removed. She saw her urologist two years ago and was told by him that her renal (right) function was good, though she denied that any special studies or tests were performed. She recalled pain in her back almost as long as she could remember. The above urinary symptoms were present before nephrectomy was done and at that time she was told that she had bladder ulcers. There had been no recurrence of the urinary tract symptoms except during the two pregnancies.

She had had the usual childhood diseases without known complications or sequelae. She had typhoid fever at the age of 14 years, was quite ill, was confined to bed for three months, and was not aware of any complications or sequelae but ten years later was told that her upper urinary tract infection resulted from this illness. The menarche occurred at the age of 18 years, menses had recurred irregularly with scant flow of only one or two days' duration, and the last period had begun 21 weeks ago with fetal movements first felt a week ago. She was a housewife with regular and good habits, had ranged in weight from 98 to 110 pounds, and says she had always tired easily and therefore limited herself to indoor activities.

Her family history was noncontributory. She had been married for 10 years and had had one previous pregnancy which had ended in the thirty-sixth week, seven years before, i.e., three years after left nephrectomy. She had had an acute flare-up of her old urinary infection beginning at mid-pregnancy. This was treated by renal pelvic lavage five times weekly with no other known therapy and none at all after delivery. Labor was induced by means of a Voorhees bag. The labor lasted 12 hours and delivery had been by forceps extraction of a 5 pound, 2 ounce living child.

On initial examination in the second pregnancy she was found to be of small stature and build. She appeared ill but fever was not high (100.6° F.). General physical examination was essentially normal. The left nephrectomy scar was obvious. There was some tenderness over the right kidney and in the corresponding costovertebral angle. Catheter

specimen of urine presented rare red blood cells, a few epithelial cells, many pus cells in clumps, and many motile bacteria from which *Escherichia coli* were cultured. Blood studies revealed anemia with hemoglobin 8.4 Gm., 2.87 million red blood cells, and 11,000 white blood cells, with fairly normal differential. Blood chemisty tests showed no retention of protein metabolites. Fractional P.S.P. test showed an appearance time of 10 minutes with considerable evidence of renal insufficiency (Fig. 4).
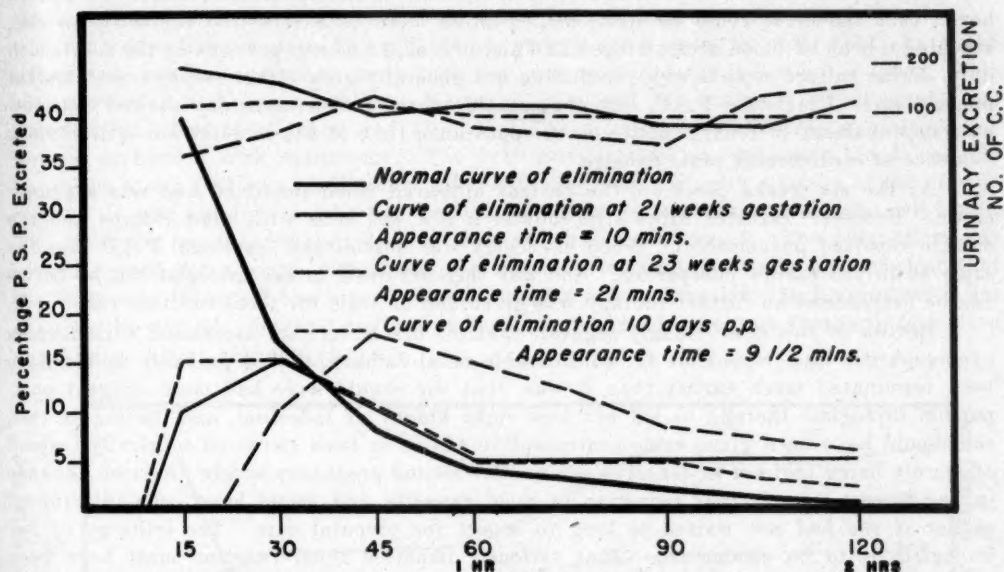

Fig. 4 (Case 3).—Patient L. H. Curves of P.S.P. elimination in the second pregnancy of a 34-year-old woman with serious infection of the lone right kidney.

Immediately after admission, sulfathiazole therapy was begun and the blood level rapidly raised to 5.4 mg. per cent, where it was maintained but after a week she developed urticaria. This was definitely proved to be due to the sulfonamide for the rash subsided rapidly upon withdrawal of the drug and reappeared three hours after the first dose given 36 hours later. However, under treatment her fever and symptoms rapidly subsided but the urine continued to show infection, pus cells decreased in number, and the urine specific gravity ranged from 1.002 to 1.015, but there was no change in the P.S.P. curve of elimination.

Two weeks after admission, she began to show retention of protein metabolites, blood urea nitrogen of 19.1, previously 13.2 mg. per cent. Fractional P.S.P. test was now unsatisfactory because, in spite of the forcing of fluids to 2,000 c.c. for two hours, the 15-minute urine output was generally inadequate. The appearance time had increased to 21 minutes and the peak of excretion of the dye shifted to the third period. Intravenous pyelography demonstrated delay in excretion of the dye, marked dilatation of the right ureter, renal pelvis, and calyces with clubbing of the latter, and kinking of the ureter. With these facts at hand, it seemed obvious that renal damage was progressing under observation and therapy, that interruption of the pregnancy was urgently indicated, and that simultaneous sterilization was in order. The consultant urologist, on the other hand, exhibited an undisturbed attitude, admitted only that continuation of pregnancy was a fit subject for debate, and believed that expectancy should be indulged in until a viable child was possible. It must be recalled that the pregnancy had now advanced into its twenty-third week. He suggested frequent check-up to detect progressive deterioration in renal function, obviously ignored the presented facts of such progression, and thought that there was not undue risk in waiting for more positive evidence of renal damage.

Accordingly, two days later under intravenous Pentothal Sodium, the pregnancy was interrupted by abdominal hysterotomy and tubal sterilization was effected by the Irving technique. Because of the persistent anemia, blood transfusion was given during operation.

The postoperative course was technically afebrile and smooth except for some distention and inadequate food and fluid intake but surprisingly good urinary output. Three days after operation, she was restarted on small doses of sulfanilamide because it was still hoped that the urine could be sterilized. Protein metabolite retention continued to rise, reaching a peak of blood urea nitrogen 25.6 and uric acid 8.65 mg. per cent on the fourteenth day. Urine culture reports were conflicting but generally grew either staphylococci and/or pneumococci. Fractional P.S.P. test done on the tenth postoperative day showed considerable improvement in renal function with appearance time of 9½ minutes but still obvious evidence of considerable renal damage.

At the six weeks check-up, the patient appeared much improved and was asymptomatic. However, catheter urine still showed a few pus cells with some clumps and the culture reported pneumococci. Blood chemistry was normal and fractional P.S.P. test the same as in the earlier puerperium. She was then returned to the urologist but so far as can be determined no further therapy was given and no tests for renal function run.

Review of this case strongly suggests that the first pregnancy associated with obvious pyelonephritis was responsible for considerable renal damage, that it probably should have been terminated much earlier than it was, that she should have had more diligent postpartum urological therapy to rid her lone right kidney of infection, and, failing in this, she should have been given some contraceptive advice or been sterilized surgically instead of merely being told not to conceive again. The second pregnancy surely produced advance in her disease, i.e., further reduction in renal capacity and would have been interrupted earlier if she had not waited so long to report for prenatal care. The lethargy of her urologists is to be condemned. That seriously impaired renal function must have been present since the first pregnancy, if not since nephrectomy, would seem to be obvious. The degree of impairment observed with the second pregnancy just beyond its mid-point suggests that any renal function test performed earlier would have proved its presence and pointed the way to taking every possible precaution to protect what renal tissue remained in this lone kidney.

CASE 4.—C. F. R. This patient was a 30-year-old, registered, white, private patient, para 1-0-0-1, with normal pelvis, negative serology, and Rh positive. She was first seen on April 1, 1943, when her second pregnancy had advanced through the sixteenth week.

Her family history is of interest only because her father died of diabetes at the age of 57 years and her mother had arteriosclerotic heart disease first noted at the age of 60 years. The patient had been married for seven years. Both she and her husband are physicians. Her previous pregnancy is said to have been normal and to have ended at term in 1940 with midforceps, Scanzoni, delivery of an 8 pound, 6 ounce child who is living and well.

Between the ages of 4 and 7 years, she had had three operations on the right kidney said to have been because of ptosis and enlargement associated with abdominal swelling. More specific medical information was not obtainable. This illness ended with right nephrectomy at the time of the third operation. Since then there had been few renal function tests, none with the previous pregnancy and none since then. Appendectomy was effected with the first kidney operation. The only serious medical illness was diphtheria one year ago. The menarche occurred at the age of 12 years and menses were within normal limits.

Physical examination revealed a medium-statured young matron in apparent good health who, at the end of 16 weeks' gestation, weighed four pounds more than her usual nonpregnant weight. She had had a little nausea in early pregnancy and it had otherwise been uneventful up to that time. General physical examination revealed no pathologic conditions. Blood pressure was 132/80. A short old right rectus scar and a longer old one in the right flank area attested to her earlier surgical experiences. The size of the uterus

corresponded to her period of amenorrhea. Pelvic measurements were normal and pelvic examination revealed normal parous findings with very good perineal and vaginal support. Complete blood count was normal and routine urinalysis showed a specific gravity of 1.015 with no proteinuria, sugar, formed elements, or bacterial organisms.

The pregnancy progressed normally except for excess weight gain on three occasions, with a total weight gain of 29 pounds, but never with edema or other signs or symptoms of toxemia except for a single blood pressure reading of 140/80. The highest diastolic reading at any time was 82 mm. Hg and urine findings were always normal.

On her estimated date of confinement, and at her request in order that she might sooner join her husband at an army base, she was admitted for induction of labor. This was successful with ergot powder. Morphine was used for analgesia when caudal was unsuccessful. Her total labor was 4½ hours and delivery was effected by elective low forceps extraction with episiotomy. The only complication was excessive blood loss due to uterine atony that was readily controlled with oxytocics and with massage of the uterine corpus. It was not followed by any detectable fall in hemoglobin or red blood cell count. The child was normal, weighed 3,550 grams, and was easily reared. The puerperium was normal except for nursing difficulties, the nipples becoming so tender and cracked that the baby was taken off the breast at the end of a week. She left the hospital with her child on the twelfth puerperal day and it has been impossible to obtain further information about her or about her renal status.
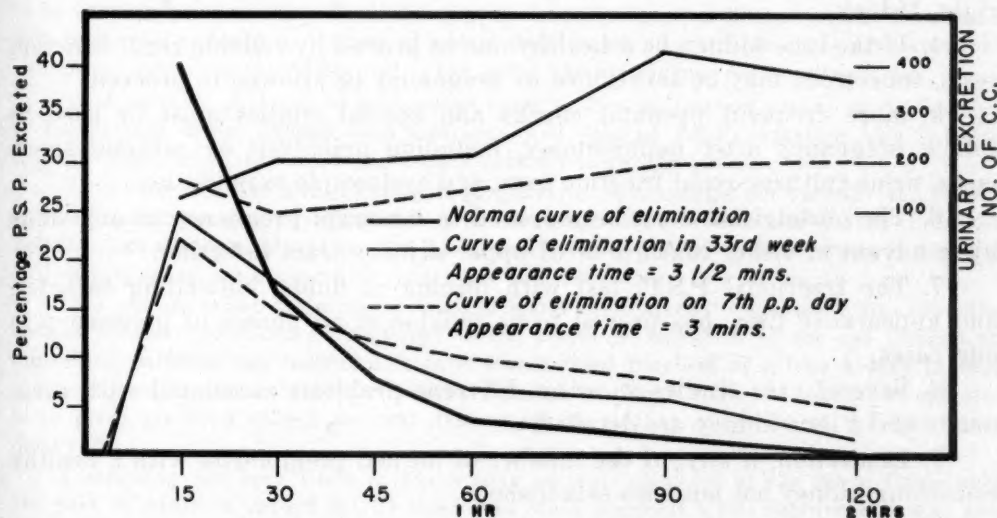

Fig. 5 (Case 4).—Patient C. F. R. Curves of P.S.P. elimination in a 30-year-old secundipara whose right kidney had been removed in childhood for unknown reasons.

During the period of observation of this patient, three fractional P.S.P. tests were obtained. The first, taken immediately after her registration, was incomplete because of technical difficulties. Sufficient information, however, was obtained to prove that her lone kidney was in good condition. A second and complete test was obtained during the thirty-third week of gestation and a similar test was done a week after delivery. These latter two appear in Fig. 5.

The curves of phenolsulphonphthalein excretion in the second pregnancy of this patient with a lone left kidney indicate barely normal or slightly subnormal renal capacity although the appearance times are well within normal limits. They make the question of future pregnancies a doubtfully safe one. It is unfortunate that neither earlier or more recent curves are available for with either it should be possible to determine conclusively whether there has been advance in loss of renal function and whether further pregnancies should be allowed.

Finally, the question of how many pregnancies a patient with a lone healthy kidney should be allowed to have, providing each is free of infection and toxemia, has not yet been answered. It is quite possible that there need be no limitations under such circumstances. Apparently, the largest number of normal term pregnancies had by any patient after nephrectomy is five as reported in one patient by King and Herring[15] and in another by Andrews quoted by Matthews.[4] In neither of these instances were any special renal function tests mentioned.

Conclusions

1. The incidence of nephrectomy, of nephrectomy during pregnancy, and of pregnancy with a lone kidney are increasing but reliable figures are not available.

2. Pregnancy should not be allowed after nephrectomy for malignancy, for congenital cystic disease, probably for tuberculosis, and in the presence of a remaining damaged kidney.

3. The risks attached to pregnancy after left nephrectomy are greater than when the left kidney is the remaining organ. Prophylactic chemotherapy against pyelitis would probably be indicated to assist in protecting the lone right kidney.

4. If the lone kidney be a healthy one as proved by reliable renal function tests, conception may be sanctioned or pregnancy be allowed to proceed.

5. More frequent prenatal checks and special studies must be used to follow pregnancy after nephrectomy, including urinalysis on catheter specimens, urine cultures, renal function tests, and cystoscopic examination.

6. The obstetrician must be prepared to interrupt pregnancy at any stage upon advent of either toxemia or of upper urinary tract infection.

7. The fractional P.S.P. test with forcing of fluids, indwelling catheter, and appearance time, has proved to be reliable in all phases of pregnancy in our cases.

8. Several case studies showing different problems associated with pregnancy and a lone kidney are detailed.

9. Limitation, if any, of the number of normal pregnancies with a healthy remaining kidney has not been established.

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Discussion

DR. ROBERT D. MUSSEY, Rochester, Minn.—Dr. Dippel's paper shows his thorough knowledge of his subject. It indicates thoughtful consideration of the plan of evaluation of renal function in the cases he is reporting. I am pleased to have the opportunity to discuss the paper.

In attempting to evaluate whether or not the renal functional is sufficient to permit pregnancy, one must be mindful of the physiologic changes resulting from pregnancy and their effect on renal function. I have had an opportunity to review renal physiology with my friend, Dr. K. G. Wakim.

The author has stated that pregnancy increases the work of the vascular-renal system; this is owing to the added load of increased metabolism and the excretion of fetal and placental products, by an increased positive water balance resulting from increased intra-abdominal pressure predisposing to disturbance of renal circulation. Intraureteral pressure is increased owing to pressure on the ureters at the pelvic brim by the enlarging uterus and to lessened ureteral peristalsis as a result of loss of tone of smooth muscle of the ureters and renal pelvic wall owing to hormonal action.

Clinical observations have shown that this added physiologic load will sometimes overburden renal function which otherwise would be sufficient to carry on in the nonpregnant individual.

I agree with Dr. Dippel that there is no single renal function test that has been found to be universally acceptable. Renal function in the nonpregnant individual can be determined with reasonable accuracy by a study of several tests, namely, the urea clearance determinations and the phenolsulphonphthalein test. The latter has the highest degree of accuracy.

Demonstrable evidence of generalized vascular disease, lowered ability of the kidneys to concentrate urine, lowered urea clearance, and delayed P.S.P. excretion may indicate that the function of the surviving kidney contraindicates pregnancy.

If the woman with a lone kidney is pregnant we have carried out vascular and retinal studies and urine concentration and urea clearance tests to evaluate kidney function. Reliance has not been placed on the P.S.P. test because urinary ureteral stasis in the last half of pregnancy has appeared to render this test inaccurate.

The author called attention to ureteral stasis in advanced pregnancy. However, the method he describes which he employed in the fractional collection of the dye through an indwelling catheter has enabled him to evaluate renal function of a lone kidney in four pregnant women. Does the Fowler position which is employed while the indwelling catheter is in place serve to relieve ureteral urinary stasis, so that collection of the dye is not delayed?

A sampling has been made of the woman patients observed at the Mayo Clinic over the past 35 years in regard to (1) those who were pregnant when nephrectomy was performed, (2) the evaluation of function of the remaining kidney in order to advise the patient concerning the risk of possible future pregnancy, and (3) the outcome of pregnancy in nephrectomized women.

Among the patients on whom nephrectomy was done in the earlier years renal tuberculosis was the leading pathologic cause and chronic infected hydronephrosis was not far behind. As time passed there has been a decided drop in the incidence of renal tuberculosis and, in more recent years, particularly since the advent of the antibiotics, the number of those with chronic renal infection was greatly lessened.

In our experience the recovery of pregnant women following nephrectomy has been generally as satisfactory as among the nonpregnant. Very few therapeutic interruptions of pregnancy have been deemed necessary before operation and few miscarriages occurred following nephrectomy.

The ability of the nephrectomized women safely to undergo subsequent pregnancy was found to depend chiefly on the extent of damage, if any, inflicted on the remaining kidney by the original disease; if the function of the remaining kidney has not been

damaged by the original disease, or impaired by conditions such as those which would curtail renal function in women with both kidneys, almost all pregnancies in nephrectomized women have been reasonably free of kidney complications.

I wish to thank Dr. Dippel for presenting a different attack on the evaluation of function of the lone kidney. Studies of additional cases will be of added interest.

DR. CLIFFORD B. LULL, Philadelphia, Pa.—Dr. Dippel has pointed out the fact that pregnancy in a patient with a lone kidney does not necessarily mean disaster. I agree with him that pregnancy should not be allowed if nephrectomy was performed for malignancy, congenital cystic disease, or most probably for tuberculosis. Certainly one of the contraindications to pregnancy would be the presence of a damaged lone kidney. The idea of treating a patient with a lone kidney prophylactically by chemotherapy to protect her from the possibility of urinary infection I believe also is indicated. If a patient who has had a nephrectomy wants to become pregnant I do not feel that the ordinary tests such as have been outlined here are sufficient and I personally would rely more on the intravenous urogram than I would on the examination of a catheterized specimen or renal function tests. Very frequently intravenous urogram demonstrates definite pathologic conditions which do not show up either with catheterized specimens, urine cultures, renal function tests, or even cystoscopic examination.

Recently I have had the opportunity of taking care of a patient who did not have an intravenous urogram preceding her pregnancy and who ran a positive test for albumin during the entire period. She did not have any symptoms of toxemia or other signs of renal impairment. After the pregnancy was terminated successfully at full term, her urologist decided to do an intravenous urogram and found an aberrant vessel around the ureter. This patient had had a nephrectomy at the age of 12 years for polycystic disease and had gone through her first pregnancy four years previous to this one without showing any kidney damage. This patient will be operated upon within the next month or two and her urological consultant feels that this will clear up the present albuminuria. Because her last child died at the age of 4 months from leucemia, she is extremely anxious to become pregnant again. If the albuminuria clears up I can see no reason why she should not be allowed to undertake another pregnancy.

I do not believe that anyone can definitely state how many pregnancies a woman with a healthy remaining kidney should undertake but from my own personal experience, if there is no damage to the remaining kidney, they go through pregnancy very well. I believe that the decision as to further childbearing should be based on the studies made on the individual patient.

DR. DIPPEL (Closing).—Dr. Mussey raises the question about whether our use of Fowler's position, which is described in the nonabbreviated manuscript, counterbalances the physiologic stasis of pregnancy in the ureter and the renal pelvis. That has been one of the serious objections in placing any great amount of reliance on the P.S.P. test during pregnancy. We think this position does counterbalance urinary stasis, we rely on it, because we have not found any alteration in the P.S.P. curve of elimination unless there was associated with it some clinical evidence of damage to the kidney. We have laid more stress upon the fractional P.S.P. test and rarely use any of the others. I think McGee and Martin's experience is of considerable importance. They found that all the tests they had used agreed in only one-third of the cases which they had tested and that the P.S.P. test gave the highest degree of accuracy.

AN EVALUATION OF CESAREAN SECTION IN INFANT MORTALITY*

CARL P. HUBER, M.D., INDIANAPOLIS, IND.

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ONE year ago the cesarean sections which had been performed at the Indiana University Medical Center during the preceding ten years were reviewed. There had been five maternal deaths and these were analyzed.[1] In the last five-year period there had been no maternal deaths. To this has been added an additional year so that from July 1, 1944, to June 30, 1950, there have been 606 cesarean sections performed at the William H. Coleman Hospital without a maternal death.

This apparent safety of the operation justifies additional evaluation before the procedure can be accepted as a satisfactory solution to a number of obstetric problems. During the past six years the incidence of cesarean section has been 5.9 per cent in our institution. This is considerably higher than in many hospitals. It is artificially raised by the fact that our staff, most of whom also practice in two other Indianapolis hospitals, by choice, bring patients to us for scheduled cesarean operations. In addition, it has been our policy to deliver patients by cesarean section who have had a previous cesarean. We believe that such a patient has a safer obstetric future if all of her pregnancies are terminated by cesarean section. There is no way that one can predict the character of the uterine scar. A weak scar is not infrequently encountered at the time of a repeat section. This is true even when there has been no infection and good technique has been used. Forty-four per cent of the cesarean sections at the Indiana University Medical Center have been repeat operations.

If a high incidence of cesarean section is associated with an absence of maternal mortality the deciding factor in its wisdom is dependent upon the infant loss. The purpose of the present investigation is to assay that factor. The infant loss during the six-year period from July 1, 1944, to June 30, 1950, has been reviewed from this point of view. The gross infant mortality for the 10,208 deliveries during this period was 36.9 per 1,000 deliveries. Fifty-nine and one-tenth per cent of these 377 infants were stillborn. Sixty-seven and two-tenths of the neonatal deaths were those of premature infants of whom more than one-half weighed less than 1,500 grams (Fig. 1).

The gross infant loss was 14.6 per 1,000 deliveries greater for cesarean section than for vaginal delivery. This is a 45 per cent greater loss in the section group and until analyzed represents a surprising discrepancy. It certainly supports the statement which is widely taught that cesarean section is no guarantee of a living infant (Fig. 2).

The delivery of a known dead infant by cesarean section is rarely necessary. Nevertheless 9 of the 28 infants in this series were stillborn. Six of them were term and three premature (Table I). Three stillborn infants were delivered of patients with complete placenta previa with sufficient blood loss so that from 1,500 to 2,500 c.c. of blood were administered before section was undertaken. None were in labor at the time. In addition, two patients with complete placental separation who were in shock were delivered of stillborn infants following repeated transfusion. Neither of these patients was in labor. One patient was delivered of a term infant who was known to be dead. She had had a previous cesarean and failed to respond to a medical induction of labor.

TABLE I. FETAL DEATHS, INDIANA UNIVERSITY MEDICAL CENTER, JULY 1, 1944, TO
JUNE 30, 1950

Fetal deaths		9
Premature	6	
Term	3	
Placenta previa		3
Abruptio placentae		2
Previous cesarean		1
Transverse presentation		1
Uterine inertia		2

The three remaining fetal deaths were associated with cesarean section performed after the onset of labor. One was the death of a fetus in transverse presentation with prolapse of the arm. The fetus was also erythroblastic and probably would not have survived an uncomplicated delivery. The second fetus was delivered following a prolonged labor complicated by uterine inertia and cervical dystocia due to previous conization of the cervix. The infant was thought to be living but was dead on delivery. The third infant in this group was delivered following a prolonged labor with delivery attempted through an incompletely dilated cervix before admission to our hospital. The infant was dead at that time and labor failed to progress. A cesarean hysterectomy was performed.

All of these cesareans with fetal loss seem justified with the possible exception of the known dead infant delivered because of a previous cesarean section.

TABLE II. NEONATAL DEATHS, INDIANA UNIVERSITY MEDICAL CENTER, JULY 1, 1944, TO
JUNE 30, 1950

	PREMATURE	TERM
Toxemia	8	
Placenta previa	2	1
Previous cesarean	4	2
Previous stillbirth		2
Neonatal deaths	14	5
Total neonatal deaths		19

The neonatal deaths which occurred in this series number 19 (Table II). All but five of these were premature infants. The indication for eight of the fourteen sections resulting in the neonatal loss of premature infants was the presence of toxemia. All patients had received conservative medical management with failure of sufficient response to justify continuing the pregnancy. None were eclamptic. The smallest of this group of infants weighed 940 grams and lived for three months. Five were under 1,500 grams at delivery. The mother of one was also a diabetic.

Two premature infants were delivered because of severe placenta previa and weighed 1,410 grams and 1,560 grams, respectively. One of the mothers was in shock at the time of admission to the hospital.

The remaining four instances of neonatal death among premature infants followed repeat cesarean section. One of these was done prematurely because of spontaneous rupture of the membranes. The other three are listed as premature infants because they weighed slightly under 2,500 grams. All were within two weeks of the calculated date of confinement. Three of these infants exhibited microscopic findings typical of the recently described hyaline membrane within the pulmonary alveoli.[2] The fourth died on the third day of a hemorrhagic pneumonitis of undetermined etiology. The occurrence of these four neonatal deaths in this group emphasizes the importance of careful evaluation of the duration of pregnancy and the size of the infant where elective repeat cesarean section is practiced. Errors of judgment in this group are tragic.

Indiana University Medical Center
July 1, 1944 - June 30, 1950

Total Deliveries · · · · 10,208
Maternal Mortality · · 1.87/1000
Infant Mortality · · · 36.9/1000

Fetal [_____] 59.1%

Neonatal | Premature | Term | 40.9%
          67%   33%

Fig. 1.

Five term infants were delivered by cesarean section and died neonatally. One was delivered of a patient with a complete placenta previa, not in labor, who was in shock on admission. Intrauterine anoxia undoubtedly irreparably damaged this infant. Two neonatal deaths occurred in infants of patients who had repeat sections before the onset of labor. One of these developed secondary atelectasis and although autopsy was not performed the development of a hyaline membrane in the lungs of this infant must be seriously considered. The other infant was anencephalic and survived only a few minutes. This occurrence which was unrecognized re-emphasizes the routine in which most of us believe, namely, that a roentgenogram should be obtained of every fetus that is to be delivered by elective cesarean section. The remaining two infants were each delivered by cesarean section because of a history of previous stillbirth following difficult vaginal delivery. Neither mother had a contracted pelvis. One was obese. One infant lived 30 hours, the other 24 hours. Autopsy was not obtained in either instance. Respiration was never normally established in either infant.

In the total group of 28 cesareans associated with infant loss, the analysis can be summarized by stating that 8 of the infant deaths were associated with the toxemias of pregnancy, 6 with placenta previa, 7 with repeat cesareans, 2 each with sections done because of abruptio placentae, uterine inertia, and previous stillbirth, and 1 because of a transverse presentation (Table III).

As we review this series and evaluate the available data it seems probable that two of the sections should not have been done. These are the one for de-

livery of the term anencephalic infant and the one for delivery of a known dead infant at term, performed following failure of medical induction because it was a repeat section. In addition, some justifiable question may be raised concerning the four repeat sections done electively and resulting in the delivery of infants weighing less than 2,500 grams. Interestingly, these six infant deaths comprise almost one-fourth of the total infant loss in the series and are in a group of patients in whom optimum results should be obtained. Eastman[3] states that rupture of the uterus occurs in 1.1 per cent of patients during labor following cesarean section. If we apply this figure to our series and assume 100 per cent fetal mortality in the event of rupture we would have lost 3 infants. There would have been other hazards in 268 vaginal deliveries which might well have raised the total infant loss above that recorded in our group.

Indiana University Medical Center
July 1, 1944 - June 30, 1950

Total Cesarean Sections · 606 (5.9%)
Maternal Mortality · · 0/1000
Infant Mortality · · 46.2/1000

Fetal		32.1%

Neonatal	Premature	Term	67.9%
	73%	27%	
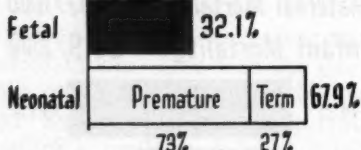
Fig. 2.

Approaching the problem from another point of view one must recognize that in any series of vaginal deliveries there are inevitably situations in which the infant might well have survived if an abdominal delivery had been performed.

In reviewing the infant loss in the entire series we have kept this point in mind. In order to avoid controversy we omit a number of infants delivered vaginally in the presence of placenta previa, abruptio placentae, and prolapse of the cord. We have also omitted all premature infants and all breech presentations. There are eight term infants who might have survived had they been delivered by cesarean section. Two of these were infants of diabetic mothers. One died in utero in the thirty-ninth week and one died in early labor at term. We also find six infants who died during the course of prolonged labor and subsequent delivery. In no instance was a contracted pelvis present. Varying degrees of uterine inertia were characteristic. All weighed between 4,000 and

TABLE III. TOTAL CESAREAN INFANT LOSS, INDIANA UNIVERSITY MEDICAL CENTER,
JULY 1, 1944, TO JUNE 30, 1950

Toxemia	8
Previous cesarean	7
Placenta previa	6
Abruptio placentae	2
Uterine inertia	2
Previous stillbirth	2
Transverse presentation	1
Total	28

5,100 grams. Errors of judgment occur during the course of vaginal delivery as well as in the decision to perform a cesarean section.

In summary, we feel that valuable lessons are to be learned by careful review of current statistical data. The magnitude of infant loss is to be emphasized. The possibility of greater infant salvage is the desired end result of such a review.

Conclusions

The following conclusions seem warranted:

1. Cesarean section when performed under proper conditions is a safe operation.

2. Maternal mortality should approach zero.

3. Infant mortality is greater than following vaginal delivery.

4. Repeat cesarean section does not increase the risk for either mother or infant.

5. The premature infant has less chance of survival following cesarean section than following vaginal delivery.

6. Careful evaluation of previous experience does not justify increasing the incidence of cesarean section.

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Discussion

DR. WARD F. SEELEY, Detroit, Mich.—It would seem to be reasonable to think on first survey that the fetal mortality rate associated with cesarean section should be low as many of the mechanical difficulties of delivery from below are entirely eliminated. Actually, however, this is not the case, for mortality rates usually varying from 4 to 8 per cent are currently reported.

Maternal mortality following cesarean has fallen sharply in the last 20 years but the fetal death rate, while showing some downward trend, has not shown the same marked improvement. Thus, in the Detroit metropolitan area in 1925, maternal mortality was 13 per cent, in 1930 4.4 per cent, and in 1945 0.8 per cent, while the fetal rates after section for the same years were 11 per cent, 12.8 per cent, and 7.8 per cent. Figures for the metropolitan area are not available since 1945, but in the following four years ending 1949 on our service at Harper Hospital the gross fetal death rate following section was 4.7 per cent.

On more careful inquiry into the causes of fetal death after cesarean it can readily be seen that many etiological factors making cesarean necessary also operate to cause fetal death. Among these are placenta previa, toxemias, abruptio placentae, ruptured uterus, all of which may also be associated with prematurity which still further endangers the fetus. We have been impressed with the better fetal salvage among prematures when cared for in a separate nursery by specially trained nurses.

It has been postulated that there are peculiar difficulties of respiratory onset in babies delivered by cesarean section. Thus Bloxsom believes that a test of labor decreases the incidence of postsection asphyxia by 25 per cent; and that failure to condition the infant by uterine contractions or passage through the birth canal is responsible for some cases of asphyxia. Landau and his associates have been impressed by babies in whom adverse symptoms do not appear at once, but are seen two to four hours later. These babies leave the operating room apparently in good condition but later develop

cyanosis and respiratory distress with costal retraction and rapid, weak pulse and usually die within eighteen to twenty hours. Similar observations have been made by Potter, whose only pathological findings were an increase in cerebrospinal fluid in the subarachnoid space. Clifford believes this is the result of anoxia and has shown it in infants delivered by section because of placenta previa, but Potter thinks it is related to the delivery by cesarean rather than to the condition for which it is done.

De Marche and his co-workers found that the immediate clamping of the cord at section deprived the fetus of an average of 107 c.c. of blood. They estimate that more than 26 per cent of the average total fetal blood is in the placenta and umbilical cord. Under normal conditions of delivery most of this blood goes to the fetal circulation during the third stage of labor. The amount received is large in relation to the total blood volume (about 360 c.c.). They believe in draining the placenta into the fetal circulation after it is removed and think the delayed reaction mentioned is really hematogenic shock. It seems possible to us that early clamping of the cord at cesarean may be a factor in high fetal mortality. In this connection it might be mentioned that Dr. Howard Kelly, as long ago as 1893, speculated on the effects on the fetus of incision through the placenta in the course of cesarean section.

Certain preoperative medication (morphine, heroin, ephedrine) may have an adverse effect upon the fetus, but this is only slight, is the belief of Pednis, Irwin, Philpotts. We have been unable to discern any significant difference in the effects of general, spinal, or local anesthesia.

As maternal mortality in our countries is coming to be under better control, more attention will undoubtedly be given to the next major problem; that of our fetal death rate, and we are indebted to Dr. Huber for presenting to us one phase of this important problem.

DR. A. W. DIDDLE, Knoxville, Tenn.—Dr. Huber has shown that cesarean section may be a relatively safe operation. To the contrary, it does not insure a lower fetal mortality than does vaginal delivery. It is my opinion that the fetal mortality with cesarean section is even greater in the average medical community than that given by the essayist. With the idea that the Knoxville area represents an average medical community, data are given to substantiate my opinion.

With the aid of Drs. K. A. O'Connor and Samuel Lambeth an obstetric survey was made among five of six civilian hospitals serving Knoxville, Oak Ridge, and Maryville, Tenn., designated hereafter as the Knoxville Area. Statistics were available for periods of 19 to 29.5 consecutive months for each hospital between Aug. 1, 1947, and June 16, 1950, with a total experience of 123 months. A total of 13,330 babies were born in the five institutions, 631, or 4.9 per cent, by cesarean section. The percentage of abdominal deliveries among the various hospitals ranged from 1.6 to 7.5. Complete mortality figures were known for 620 infants. Sixty-four, or 10.3 per cent, of these babies were either stillborn or died before discharge from the hospital. Compare this percentage to 4.6 given by Dr. Huber. Complete information correlating the indication for abdominal delivery with fetal loss was known for 557 babies. Only about one-fourth of the deaths occurred where at least one of the indications for laparotomy was a previous section. Nearly one-half of the fetal deaths were among babies where placenta previa or premature separation of the normally implanted placenta was the primary indication for abdominal delivery. Analyzed in another way, 45 per cent of the women sectioned for bleeding lost their babies as did one in five of the women with toxemia treated by cesarean section. Where the procedure was elected without an apparent legitimate indication, the loss was nearly 5 per cent. Where there was fetal loss it was frequently known ante partum that the infant was either dead or of nonviable size. Yet, in spite of this information, abdominal delivery was elected even when vaginal delivery would have sufficed for the safety of the mother.

The combined and uncorrected stillbirth and neonatal death rate for all births in the Knoxville Area was about 38 per thousand at the end of the first year of life, while

that for the hospitals ranged from about 32 to 37 per thousand by the time the babies were discharged from the hospital. For the same time interval the rate was 103 per thousand among babies born by the abdominal route.

Fetal loss among women treated by cesarean section accounted for nearly one in five of all fetal losses in the Knoxville Area. Much of this was due to prematurity which was correlated with the fetal loss in three hospitals admitting private patients. Any baby weighing 5.5 pounds or less was considered premature. Among babies born by section the percentage of prematurity in the three hospitals was 5.4, 15.2, and 18, respectively. It was about three times as common among infants born by the abdominal route as among babies born by the vaginal route in two hospitals while in the third one the rate was nearly equal. The hospital having the lowest rate of prematurity among babies delivered by section also had the lowest rate of prematurity for all births (5.2 per cent), the lowest total fetal loss, the lowest incidence of abdominal delivery and the most careful selection of patients for cesarean section. In contrast, the two hospitals with the higher rates of prematurity among babies born by the abdominal route also had the highest rate of prematurity for all births (6 to 6.6 per cent), the highest fetal loss, the highest incidence of cesarean section, and the lowest standards for electing abdominal delivery. These studies indicate that often the factor of fetal salvage was not weighed properly in selecting cesarean section as a method of delivery.

Opposed to Dr. Huber's experience with no maternal mortality there were three deaths in this study, one each from infection, abruptio, and uterine rupture. Besides the woman who died of a uterine rupture, five others survived this complication. Five of the six patients with uterine rupture were sectioned previously. The moral is that the hazard of this complication, especially after a previous cesarean section, remains with us. It emphasizes the need for a reasonable justification to do the first abdominal delivery.

DR. FRED J. HOFMEISTER, Milwaukee, Wis.—Since we are conducting a similar study in a private institution, Milwaukee Hospital, I am very interested in Dr. Huber's paper. We have reviewed 20,157 deliveries in the ten-year period, 1940-1950. There were 1,145 cesarean sections, a rate of 5.6 per cent, with a repeat cesarean section incidence of 40.6 per cent. There were no maternal deaths associated with sections during this period. The fetal wastage for the entire series of deliveries was 633 deaths, an incidence of 3.14 per cent. Thirty-eight neonatal deaths and 24 stillbirths were associated with sections, a fetal mortality rate in cesareans of 5.4 per cent. Seventy-five per cent of these neonatal deaths were associated with prematurity and 55 per cent of the stillborn infants were premature. It is interesting to note that in every instance where a mature infant was delivered by an elected repeat cesarean section, there was no neonatal death, but there were 8 premature neonatal deaths. Three, or about 40 per cent, of these premature neonatal deaths were the result of inaccurate judgment on the part of the operators. They had erroneously considered the patient to be at or near term. The other neonatal deaths of premature infants were due to exciting factors such as abruptio, placenta previa, etc. Of the 24 stillbirths, one was associated with a repeat section and was necessitated by the occurrence of a premature separation of the placenta with massive hemorrhage.

DR. E. L. KING, New Orleans, La.—We have found that abstaining from any anesthetic drugs before section and immediate aspiration of the baby's trachea with the DeLee tracheal catheter gives us much better results.

DR. HUBER (Closing).—I had expected that such a series of infant losses would have been criticized. It is reassuring that the statistics reported by the discussants are very similar to our own experience. These data all emphasize the necessity of careful evaluation of the risk for the infant, as well as for the mother, in undertaking a cesarean section. Critical analysis of our own series has proved very enlightening.

Original Communications

THE BENIGN DIFFUSE ENLARGEMENT OF THE UTERUS

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IT WAS my opinion that the subject of the diffusely enlarged uterus had been cleared up for a good many years. Three distinct lesions were described by William Fletcher Shaw,[2] namely, (1) chronic subinvolution, (2) chronic metritis, and (3) hypertrophy. Prior to this, more or less in blanket form, the term fibrosis uteri was applied generally to designate these diffusely enlarged uteri in the absence of new growth. Shaw's principal articles appeared in 1914 and 1917. He pointed out that fibrosis suggested an increase in connective tissue, and pointed out that in clear-cut cases of chronic subinvolution, which comprise well over 70 per cent of these enlarged uteri, there is no increase in connective tissue whatsoever. Thus fibrosis is a misnomer. In chronic metritis, however, there is a definite increase in connective tissue. This at times is so marked that the connective tissue content is greater than that of the muscle tissue. The incidence of chronic metritis as compared to chronic subinvolution is rather low, comprising only about 15 per cent of all specimens. Hypertrophy, in its exclusive form, is even less common, and here again as in the case of chronic subinvolution there is no increase in connective tissue.

In 1918, I confirmed the work of Shaw and considered his classification most acceptable. However, I brought out some additional points which Shaw by way of personal correspondence accepted: First, these lesions may occur in the same uterus at the same time, most commonly two of them. Usually, however, you find them singly. Second, edema and a sort of liquefaction are present, especially in the subinvoluted uteri. This is seen most pronouncedly at the area at the junction of the middle and outer thirds of the uterus. The liquefaction is not unlike that seen in myomas, but in moderate degree, and at times, even, there is some hyaline change.

One might say that diffuse adenomyosis of the uterus is a benign diffuse enlargement. It is usually discussed with endometriosis in general. The symptomatology is somewhat different, such as pain which may be considerably increased in the postmenstrual period in some of the cases. Also dysmenorrhea and increased bleeding are usually more prominent.

The symptoms and signs of these benign enlargements are usually mentioned as increased bleeding, pelvic pain, and leucorrhea. Pain is more or less constant, frequently varying from not more than a rather definite discomfort to

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†Deceased Aug. 19, 1950.

actual pain. Backache and a dragging sensation in the pelvis are frequently described. These nagging conditions, which result from underlying pathological lesions, become more pronounced as the menopause is approached, and carry with them a train of nervous disorders, which may vary from minor complaints to full-blown neuroses.

There are women who have these symptoms and signs pointing to the pelvis, without any demonstrable enlargement or malposition of the uterus. These may well be the cases where pelvic circulatory disturbances come into play, where the uterus to all knowledge may be entirely normal.

Recently, Taylor[6] has come out with a series of articles concerning benign enlargement of the uterus: (1) vascular congestion and hyperemia, (2) the congestion-fibrosis syndrome, and (3) etiology and therapy.

In these presentations, Taylor discusses chiefly signs and symptoms without recognizing specifically definite pathological pictures which may exist in the uteri of the patients under discussion.
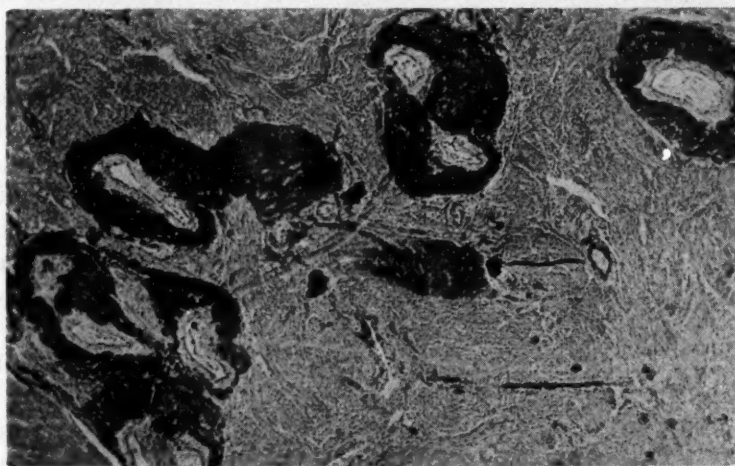
Fig. 1.—Chronic subinvolution. Artery, inner third, orcein van Gieson stain. Note the black collars around the sharp new vessel with a fine internal elastic membrane. The black material stains actually brownish black, and consists of degenerated material of the old vessel wall, muscle tissue, connective tissue, and elastic tissue. In its unabsorbed state this dead material peculiarly stains as elastic tissue, the same sort of material being seen around the veins, in between the muscle bundles of the outer third. Background, light stains, yellow muscle tissue, no increase in connective tissue which would be present in black stain.

We thought the old term of fibrosis uteri had been discarded, but now Taylor brings it back in rather loose fashion as "congestion fibrosis," fibrosis indicating an increase in connective tissue. In the absence of previous or chronic infection, there is no increase in the connective tissue of the uterus. For a period of about six years our routine uterine sections were stained both with hematoxylin and eosin and orcein van Gieson. In chronic subinvolution and hypertrophy, that is, in clear-cut cases, there is no increase in connective tissue, but in chronic metritis there is, often very markedly so. Chronic metritis, however, appears approximately, as we have said, in only about 15 per cent of these large uteri.

It must be remembered that, after the menopause, the uterus slowly atrophies, the vessels become markedly sclerotic, the muscle tissue diminishes, the fibrous tissue skeleton remaining. This, however, does not mean an increase in fibrous tissue, as there is no proliferation as, for example, in cirrhosis of the liver.

Since Taylor, in bringing forth his ideas of congestion fibrosis, did not allude to the pathologic descriptions which cover the vast majority of these enlarged uteri, we feel it would be quite proper to re-emphasize these pathologic pictures. It must also be remembered concerning chronic subinvolution, which represents roughly 80 per cent of the material, meticulous postpartum care should do much to lower the incidence of this entity, which can become most troublesome in many instances in the menopausal years. This we pointed out over thirty years ago.

We would like to bring up the pathological descriptions of these lesions again, accompanied by well-selected illustrations of clear-cut cases. Thus the gynecologist who may be interested can evaluate the two viewpoints expressed, gaining information from both, and not discarding the well-established older pathologic theories for ideas which seem to me in need of a good deal more thought before they are accepted dogmatically.

The story of chronic subinvolution begins with a masterful monograph of the late Dr. Goodall[1] on the *Normal Involution of the Circulatory System of the Uterus Following Childbirth*, published in 1910.

For many years my original illustrations concerning this condition were used in Crossen's textbook.[5] The descriptions accompanying were not entirely satisfactory. More recently Novak,[4] in his textbook, *Obstetrical and Gynecological Pathology*, treats the subject quite adequately. These are the only textbooks to my knowledge that discuss the subject in any detail.

Then in 1914 and 1917 came the original work of Shaw to which we have already referred.

Here I shall review Dr. Goodall's findings in normal involution of the circulatory system of the uterus, followed by a description of the pathology of chronic subinvolution, chronic metritis, and hypertrophy.

1. After the placenta has been expelled, the uterus contracts and compresses the markedly dilated uterine vessels which promptly attempt to reduce their caliber; this concerns especially the vessels of the inner third of the uterus at the former placental site. Here the arterial wall swells up and undergoes dissolution, the intima swells, the internal elastic membranes break up, and the muscle becomes disintegrated. In a comparatively short time, about ten days, these vessels are seen when stained (orcein van Gieson stain) which shows the elastic tissue brown-black, the muscle yellow, and the connective tissue red. At this stage the vessel appears as a homogenous mass, an intermingling of elastic tissue, muscle, and fibrous, staining a port-wine red. As time goes on and disintegration becomes more advanced, it stains a yellowish red, and finally before complete absorption, a pale yellow. While this is going on a new vessel sprouts, a continuation of the arteries of the middle third. They make their way into the lumen of the old vessel wall which surrounds the very small new vessels like a collar. If absorption of the old wall is complete, the new vessel stands out in clear-cut relief, but this absorption is not entirely complete and small tags of the

old vessel can be seen adjacent to the new vessel. As a result of this, a multiparous, or rather a former parous uterus, can be identified from a nulliparous uterus. When absorption of the old artery does not take place and when we see this to a marked degree, we see the first picture of chronic subinvolution. These areas are identified by the fact that, when they are not absorbed, and in their conglomeration, they vary peculiarly with orcein van Gieson stain, a brownish black color, similar to elastic tissue. It is not elastic but a dead material which can be regarded more or less as a foreign body. The process of involution of the arteries takes from two months to four months; hence, the importance of proper postpartum care during this period.

Fig. 2.
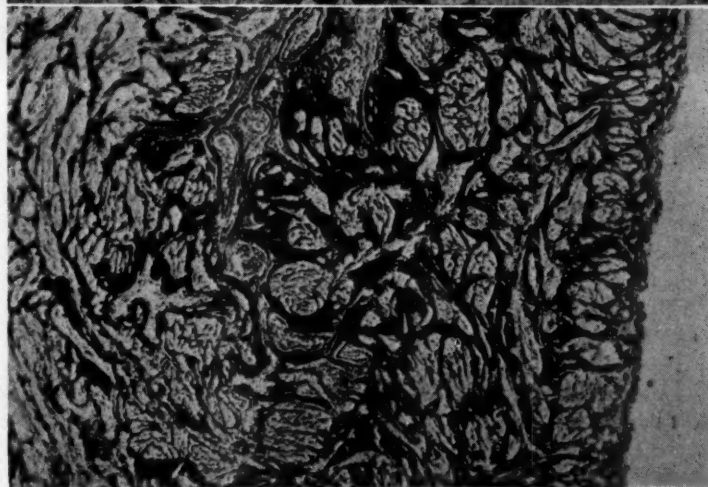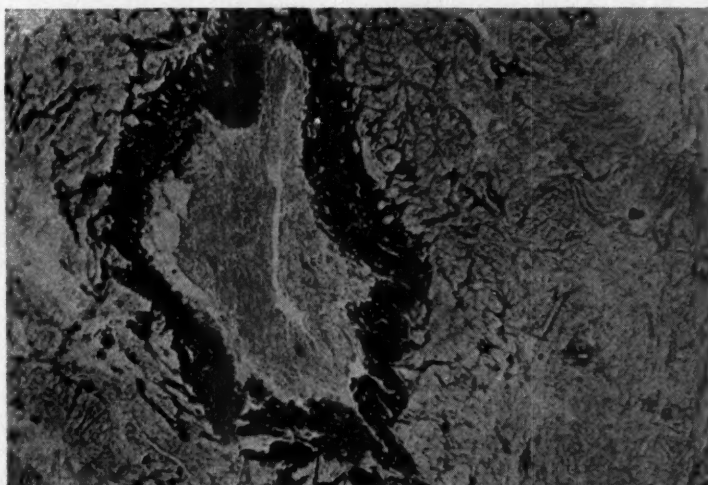
Fig. 3.

Fig. 2.—Chronic subinvolution. Vein, middle third, showing elastic tissue-like material, that is, it stains as elastic but is the same sort of dead material as in the artery. When the vein and the artery in Fig. 3 reach this stage, the material is there permanently and does not absorb later.

Fig. 3.—Chronic subinvolution. Peritoneal surface, interstitial spaces. Orcein van Gieson stain. Dark brown-black material is degenerated material unabsorbed during involution. If it were connective tissue it would also be black in the picture, but in the stained slide connective tissue is pictured. (Color photographs, which we have in lantern slides, show this beautifully.)

In the veins the process is entirely different. A comparatively small number undergo thrombosis. The remaining very large veins are compressed by the uterine wall and have markedly thickened walls and assume all sorts of bizarre shapes. The vein has no internal elastic membrane, but has a considerable amount of diffusely placed elastic tissue in the wall, which is most marked at the periphery and is sometimes referred to as an external elastic membrane. The wall in involution undergoes disintegration, but not completely so, the new wall arising from unchanged muscle, fibrous, and elastic tissue in situ. The disintegrated tissue becomes confluent and is absorbed. As a result of this the vein stains a port-wine red in the earlier part of this change. This material makes its way to the periphery of the vein where final absorption takes place. If this absorption is not complete, this same peculiar staining property takes place in the artery, the dead confluent material staining a brownish-black color and it is strikingly seen at the periphery in the form of numerous masses.
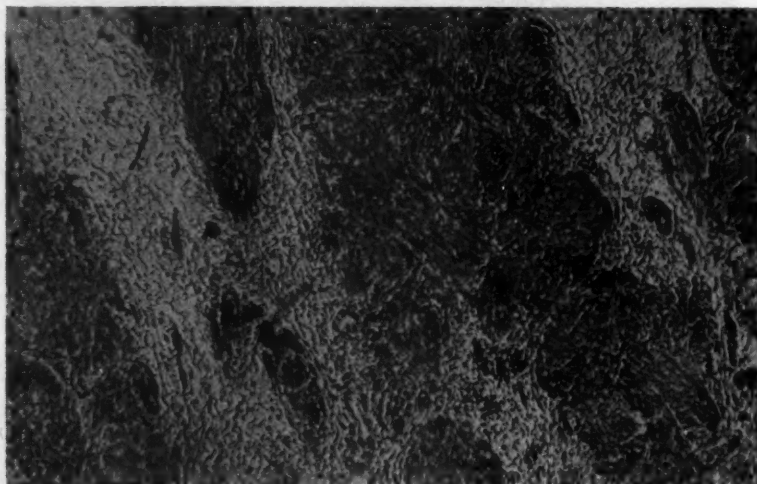
Fig. 4.—Chronic subinvolution. Junction of middle and outer thirds of myometrium, light areas show marked amount of edema with separation of muscle bundles. This picture is frequently seen in chronic subinvolution.

Pathology of Chronic Subinvolution.—Grossly the uterus is usually definitely enlarged 25 to 100 per cent, sometimes being twice the normal size. On cut surface small projections appear. With orcein van Gieson stain the arterioles of the arteries of the inner third are seen either with complete brownish-black collars surrounding them or as large tags of the same staining material which represent the whole unabsorbed old artery or its remnants. These are the old subinvoluted vessels. In the vein the wall per se is thickened, this dead tissue appearing in the wall, but more especially in the periphery of the vein and infiltrated into the interstitial spaces immediately adjacent. This dead confluent material as in the case of the artery stains a deep brown-black color with orcein van Gieson stain. This same dead material with similar staining properties appears in the interstitial spaces in the outer third of the uterus. These spaces contain fibrous tissue and a considerable amount of elastic tissue. During pregnancy, they increase in amount; in other words, they hypertrophy, and during involution much of this tissue is absorbed. As in the case of the artery and the vein, if absorption does not take place to any great degree, the dead tissue remains permanently and stains similarly.

Chronic Metritis.—The uterus is only moderately enlarged. The cut surface is smooth, and the silvery strands against the duller muscle tissue indicate in-

creased fibrous tissue. With special staining this can readily be brought out. Normally, the upper uterine wall has a ratio of muscle tissue to fibrous tissue of approximately 80 to 20. In marked cases of chronic metritis this can be almost reversed. Histologically, one sees a diffusion of small round cells and plasma cells throughout the wall. The increase in fibrous tissue can be readily seen by the marked increase in red staining material with van Gieson stain, indicating fibrous tissue.

Fig. 5.—Chronic metritis. Hematoxylin and eosin. A marked infiltration of inflammatory cells throughout the myometrium. These are chiefly small round cells though one sees a sprinkling of plasma cells. In long-standing cases the plasma cells become less prominent. This condition is almost always secondary and results after general pelvic endometritis, and endometritis associated with salpingitis; in other words it is usually a part of a general picture.
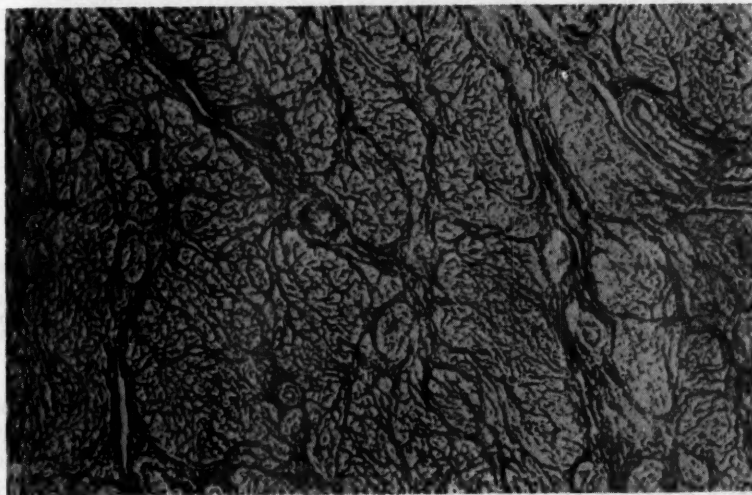
Fig. 6.—Chronic metritis. Orcein van Gieson. The black material is the markedly increased connective tissue. In the section it appears bright red against the yellow background of smooth muscle. Note how the connective is working its way between small muscle strands. In some sections this is so striking that the muscle strands actually appear to be choked off.

Hypertrophy.—This lesion also has its distinct features. The uterus may be moderately or considerably enlarged. This enlargement is usually associated with a hyperplasia of the endometrium. In some instances the uterus is twice the normal size. On microscopic examination the relationship of the muscle to connective tissue is as in the normal uterus. There is an increase in the number of cells as well as an increase in their size. I believe that many cases of so-called diffuse adenomyosis of the uterus have passed through this stage.
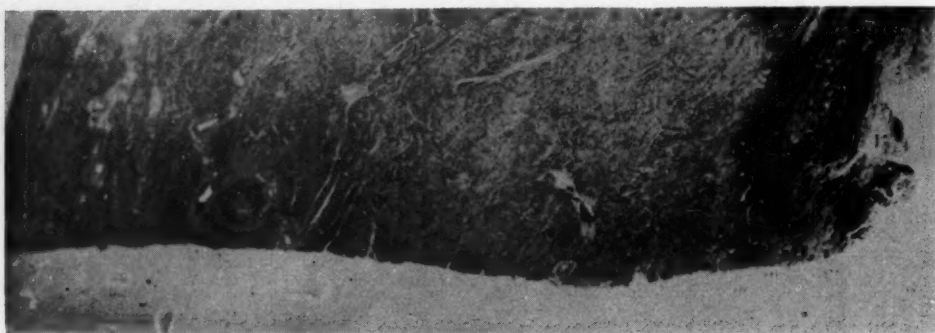
Fig. 7.—Hypertrophy. Uterus twice normal size that of an 18-year-old, nulliparous girl. On cut section the surface appears coarse, somewhat like the surface in a csae of diffuse adenomyosis, but involving the entire uterus. The muscle bundles are coarse, and the interstitial connective tissue less compact.

Fig. 8.—Hypertrophy. Orcein van Gieson stain. Section in myometrium at junction with endometrium. Inner third of myometrium. First note blood vessels, normal, precise internal elastic membrane. The fine black-streaked material is connective tissue which of course stained red. The relationship of muscle to connective tissue in hypertrophy is normal. This is normal. Compare it to the markedly increased amount in chronic metritis in Fig. 6 and to the strikingly inconspicuous amount in chronic subinvolution in Fig. 3.

Although this condition is rare in its extreme form, one of the most striking examples of this lesion was in a uterus presented to me by the late Dr. Edward Murphy of St. John's Hospital in St. Louis. This specimen is illustrated in Dr. Crossen's *Diseases of Women*. The patient was an 18-year-old girl with a history of marked menorrhagia. On bimanual examination on a nulliparous woman, the uterus was twice normal size. Dr. Murphy curetted, and obtained soft, spongy tissue, gray in color, that to him appeared as sarcoma. He did an immediate complete hysterectomy and presented me with the specimen. On ex-

amination, in spite of his curettement, there remained about 1 cm. thickness of endometrium which showed typical hyperplasia. The uterine wall was 2.5 cm. thick, loose in texture, and microscopically answered all the requirements of the picture of hypertrophy. It was the most striking example of this condition that I have ever seen.

Finally, a word concerning the clinical aspects of chronic subinvolution, which can be handled more or less from the standpoint of prevention. Naturally, meticulous postpartum care is most important. As the involution of the circulatory system to its fullest extent prevents subinvolution, and as chronic subinvolution chiefly results in permanent conditions produced by lack of involution of the uterine arteries and veins, therefore, the position of the uterus becomes all important. This should be watched for at least four months, when involution changes in the vessels are definitely complete. A pessary should be put in place whenever the uterus is back during this period; if it returns posteriorly then it will not retard involution. Today, with the early rising, pelvic circulation should be stimulated. It is conceivable that this may help the early changes, and the pessary take care of the later. But today, more than before, even in privileged groups, proper rest in the puerperium will be lacking to a greater degree. Ultimately, if the lesion is pronounced enough and the symptoms sufficiently severe complete abdominal or vaginal hysterectomy will do much toward relief.

To bring out the distinct features of each lesion, one must select cases for pictures where the particular lesion is present alone and in striking manner. Therefore, in selected cases of chronic metritis and hypertrophy nulliparous uteri are desirable as they will show no vessel changes, which any parous uterus will show, though in a minor degree, not marked enough to call it subinvolution.

I have corrected the illustrations as to the microscopic picture; for gross specimens consult references of Shaw and Schwarz.

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GROSS ABNORMALITIES OF THE PLACENTA ASSOCIATED WITH BLEEDING IN PREGNANCY

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THE purpose of this paper is to present a case of velamentous insertion of the umbilical cord with vasa previa, a condition which is accepted as a cause of bleeding in pregnancy; a second case in which we identified the bleeding site in a ruptured marginal vein; another where the bleeding occurred at the battledore insertion of the umbilical cord; and several others in which the bleeding may have been related to gross abnormalities of the placenta; and, finally, to compare the incidence of this group of cases to the number of cases diagnosed as placenta previa or retroplacental hemorrhage in a series of deliveries.

In 1927, Williams,[1] writing on circumvallate placenta, remarked that "the literature abounded in contradictory statements upon every point whether anatomic or clinical." He then went on to say, "the majority of writers have asserted that the condition may give rise to serious clinical complications such as abortion, inexplicable uterine hemorrhage, premature labor, etc.," and concluded with his own impression that the condition is practically without clinical significance.

The same contradictions are present in the literature today.

Vogt[2] (1943) considered vasa previa "a clinically important condition." He described a case of bleeding in which he thought that failure to perform a vaginal examination before cesarean section had "indirectly saved the baby's life." The preoperative diagnosis was placenta previa; if a vaginal examination had been made the patient would have been allowed to deliver normally with probable fetal death.

Records,[3] (1940) reporting a case of velamentous insertion advised that the condition should be suspected when moderate bleeding and signs of fetal embarrassment appear at term with no evidence of placenta previa or premature separation.

Describing placental anomalies of this nature Novak[4] says that "clinically only the marginal and velamentous insertions are significant."

On the other hand De Lee[5] stated that circumvallate placenta has some clinical significance, but "battledore placenta has no clinical importance." He said velamentous insertion is often found with other anomalies of the placenta, and considered this condition to be dangerous to the child only when the vessels run across the lower uterine segment.

However, Kosmak[6] (1922) reported a case of hemorrhage and a dead baby delivered by cesarean section where "the velamentous cord was inserted at the upper pole of the placenta."

On May 15, 1947, Mrs. K. was admitted to hospital with painless vaginal bleeding. She was a para ii, due June 18. Several hours later she started in labor, and by rectal examination a dilating cervix with a large bag of forewaters was palpated. A vaginal examination was made and the membranes ruptured, followed by spontaneous delivery of a baby in good condition.

A second fetal sac then presented. The umbilical vessels could be seen between the membranes overlying the head, they were not torn nor bleeding. The membranes were ruptured medially and the part containing the vessels pushed to the right over the head. Delivery was completed by low forceps.

Circumvallate

Battledore
Insertion

Velamentous Insertion
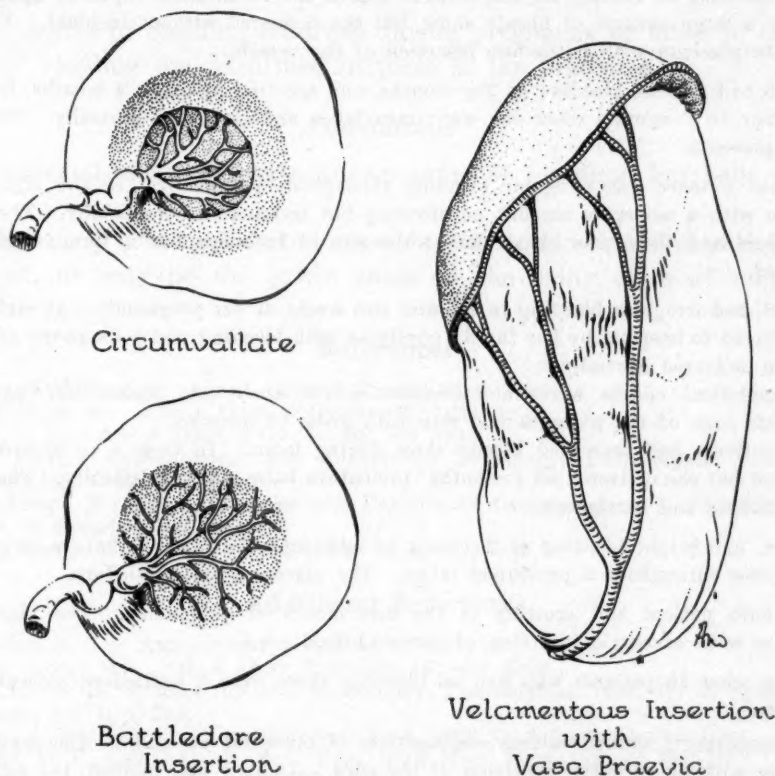with
Vasa Praevia

Fig. 1.

This baby was limp and pale but breathed and cried spontaneously after a short interval.

On examination of the placenta the velamentous vessels were found to run for about ten inches between the membranes and were intact. Where they entered the margin of the placenta there was a ruptured vessel with evidence of recent bleeding.

Mrs. C. bled suddenly and profusely at the onset of labor to the point of shock. She was delivered by classical cesarean section without previous vaginal examination. The placenta was on the anterior wall of the uterus well above the cervix which was thin and 2 to 3 cm. dilated.

Inspection of the placenta showed a small amount of blood clot overlying the membranes adjacent to one edge, and close examination indicated a torn vessel at the margin of the placental tissue with a blood clot projecting from one free end. The insertion of the umbilical cord was near this border of the placenta.

The third patient had her last menstrual period on May 15, followed by spotting from the end of May to July 30.

On January 1 there was some bright red bleeding which subsided with bed rest.

January 11 there was a sudden onset of profuse painless bleeding. The character of the bleeding was a continuous bright red profuse flow. Cesarean section was performed without vaginal examination. The placenta was on the posterior uterine wall, low lying but not extending down to the cervix.

Examination of the placenta revealed a battledore insertion of the umbilical vessels. At this site there was an indentation of the placental margin and blood clot overlay this area of the placenta and membranes but no ruptured vessel was identified.

Mrs. H. bled in varying amounts throughout her pregnancy, and appeared to be constantly threatening to abort. At the seventh month the membranes ruptured spontaneously followed by a large amount of bloody show, but she delivered without incident. This was a circumvallate placenta with battledore insertion of the vessels.

Case 5 had profuse bleeding at 2½ months, and spotting again at 4 months, but carried the pregnancy to 7 months when she went into labor and delivered normally. This was a battledore placenta.

In Case 6 there was irregular bleeding throughout pregnancy. In the eighth month labor began with a moderate amount of bleeding but terminated successfully. The placenta was battledore and there was blood clot at the site of insertion but a torn vessel was not demonstrated.

Mrs. S. had irregular bleeding in the first two weeks of her pregnancy. At eight months she was referred to hospital by her family physician with bleeding and a diagnosis of placenta previa. She delivered normally.

The umbilical vessels were intervelamentous for about 1½ inches but were intact. However, this edge of the placenta was thin with areas of necrosis.

Two patients had increased bloody show during labor. In Case 8 it occurred at the onset of labor but she delivered an 8 months' premature baby without difficulty. The placenta was circumvallate and battledore.

Mrs. A. had bright bleeding at the onset of labor and continued to have a large amount of bloody show throughout a prolonged labor. The placenta was battledore.

The tenth patient had spotting in the first month of pregnancy. The placenta was circumvallate with excentric insertion of the umbilical cord.

Of the other 10 patients who had no bleeding there were 3 battledore placentas and 2 circumvallate.

The remaining 5 showed various combinations of placental anomalies. One was partially circumvallate with an excentric insertion of the cord. Another was bilobed, the smaller lobe being circumvallate. One was bilobed, one lobe being partially circumvallate with a battledore insertion in the same area.

The last two were similar. Both placentas were battledore. In one a vessel traversed the membranes in a loop for 3 inches at the edge of insertion, and in the other for 5 inches along the placental margin.

TABLE I. A COMPARISON OF THE POSSIBLE CAUSES OF BLEEDING IN 445 DELIVERIES

CONDITIONS	NUMBER	
Deliveries	445	
Placental anomalies	20	4.27 per cent
Anomalies associated with bleeding	10	50.00 per cent of anomalies
		2.24 per cent of deliveries
Placenta previa	1	0.22 per cent of deliveries
Retroplacental hemorrhage	1	0.22 per cent of deliveries

There were 20 placentas of these various types in 445 deliveries, an incidence of 4.27 per cent. Ten of the 20 patients, or 50 per cent, had had some form of abnormal bleeding in labor or during pregnancy. In other words, in a total of 445 deliveries, 10 patients, or 2.24 per cent, had bleeding associated with abnormal placentas. In this same number of deliveries there was one diagnosed placenta previa and one case of retroplacental hemorrhage, a 0.22 per cent incidence in each instance.

Summary

A case of vasa previa is reported, eight cases of battledore placentas, and one circumvallate placenta. Five patients were multiparous and five were primiparous.

Some degree of bleeding occurred during pregnancy or labor in each case. The site of bleeding was identified in three of the placentas.

Conclusions

1. Abnormal placentas are a known cause of bleeding, but believed to be rare.

2. They may be an associated cause in placenta previa and retroplacental hemorrhage, or may be the prime cause in the many cases of undiagnosed bleeding.

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495 PRINCE ARTHUR STREET, W.

VERATRUM VIRIDE IN THE TREATMENT OF ECLAMPSIA*

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THE vast number of papers and monographs which have appeared on the toxemia of pregnancy indicate the confusion that surrounds the cause and treatment of this syndrome. Many of the treatments proposed have met with some degree of success but the results reported with veratrum viride in combination with magnesium sulfate and hypertonic glucose, since the revival of interest in this drug by Bryant and Fleming,[1] have been particularly noteworthy.

At the Maternity Hospital, University Hospitals of Cleveland, as in other clinics, this drug was used many years ago but gradually fell into discard. In 1945 its use was revived and a significant reduction of eclampsia mortality ensued. These results are believed favorable enough to add to the reports which are gradually appearing in the literature.

Incidence.—Table I shows the fifteen-year incidence of eclampsia and toxemias of all kinds among 59,488 hospital and home deliveries. The occurrence of one case of eclampsia in every 490 deliveries compares favorably with the incidences reported from other obstetrical centers. Although there was some variation in annual incidence, the same constant range was maintained and no decrease in incidence could be demonstrated.

TABLE I. INCIDENCE OF TOXEMIA AND ECLAMPSIA, MATERNITY HOSPITAL, UNIVERSITY HOSPITALS OF CLEVELAND, 1930-1945

	DELIVERIES	CASES OF TOXEMIA	CASES OF ECLAMPSIA	INCIDENCE OF ECLAMPSIA
Hospital	35,640	1,756	121	
Home	23,848	2,206		
Total	59,488	3,962	121	1:490

Role of Veratrum Viride in Treatment.—Veratrum viride is not considered to be a cure or specific but its twofold action of reducing blood pressure and heart rate is peculiarly suited to the treatment of eclampsia, for it attacks the vicious circle of the syndrome at its most basic known level, that of arteriolar spasm. This action has been found to be the result of generalized vasodilation and vagal stimulation by Willson and Smith[2] and Krayer, Moe, and Mendez[3] who have also demonstrated that the drug has no direct action, toxic, or otherwise, on the myocardium.

The studies of Willson[2] showed a reduction of urinary output following the administration of veratrum viride and suggested that the drug might be contraindicated in the treatment of eclampsia. We followed nine cases with urea clearance studies† to determine whether there was any impairment of renal

*Presented before the Academy of Medicine of Cleveland, Obstetrical and Gynecological Section, April 18, 1950.

†Six of the urea clearance studies were done at University Hospitals of Cleveland, three at Bethesda Hospital, Cincinnati.

function. Fig. 1 shows that there was a decrease in urea clearance following the administration of veratrum viride, but when combined with magnesium sulfate and hypertonic glucose there was a return of urea clearance to its original levels.

From these data we believe that the decrease in urea clearance does not in itself constitute an alarming state, because the drop in urea clearance is not great and there is a return to the original level soon after. It is probable that the initial action of veratrum viride is the production of hypotension causing oliguria and increasing the back hypodiffusion of urea; while, with magnesium sulfate and hypertonic glucose, the action is that of osmotic diuretics decreasing urea readsorption. When combined treatment is used, therefore, there is a definite improvement in urea clearance and urinary output.

Method

The method by which we employ veratrum viride is essentially that described by Bryant and Fleming,[1] except that its use is not necessarily routine in our clinic. Some patients are treated with magnesium sulfate, sedation, ammonium chloride, salt-poor diet, and rest.

In any case, blood urea nitrogen, nonprotein nitrogen, urea clearance, plasma proteins, albumin-globulin ratio, cell volume, plasma chlorides, complete blood count, and urinalysis are obtained. Other studies are carried out as indicated.

All medication is administered by the resident or an assistant resident if he has been sufficiently trained in the regime. Blood pressure and pulse are taken frequently before and after the administration of veratrum. *House officers must stay with the patient until she is definitely under control.* Veratrone (extracted alkaloids of veratrum viride, Parke, Davis & Company) is given hypodermically in doses varying from 3 to 10 minims, together with 50 per cent magnesium sulfate intramuscularly and 20 per cent glucose intravenously. Oxygen is administered by mask if necessary. When the patient will tolerate it, she is placed on a high-protein, salt-poor diet. Vitamin B complex is used when feasible. Each patient is watched and treated individually, for the variation in susceptibility to the drug precludes a rigidly standardized regime. When adequate control of the toxemia symptoms is obtained, delivery by the least traumatic means is carried out. Cesarean section is used where there are signs of cephalopelvic disproportion, premature separation of the placenta, in elderly primiparas, placenta previa, and other indications which warrant section. On the other hand, if vaginal delivery is the most expedient, this method is preferred. The same regime of veratrum viride, magnesium sulfate, and hypertonic glucose is continued in the postpartum period until recovery.

Results

Table II shows a comparison of eclampsia mortality before and after veratrum viride was incorporated into the treatment. During the fifteen-year period from 1930 through 1944 there were 15 deaths in 121 cases of eclampsia, for a mortality of 12.9 per cent. These cases were treated primarily with morphine sedation and were frequently interrupted by cesarean section. From 1945 to 1950, 34 cases of eclampsia were treated, with one death, for a mortality of 2.9 per cent. Veratrum was used in 25 of these cases, the remainder being less severe and controlled easily with sedation and/or magnesium sulfate without veratrum. Considering only the cases in which veratrum was used, there was one death in 25 cases, a mortality of 4 per cent, still a marked reduction.
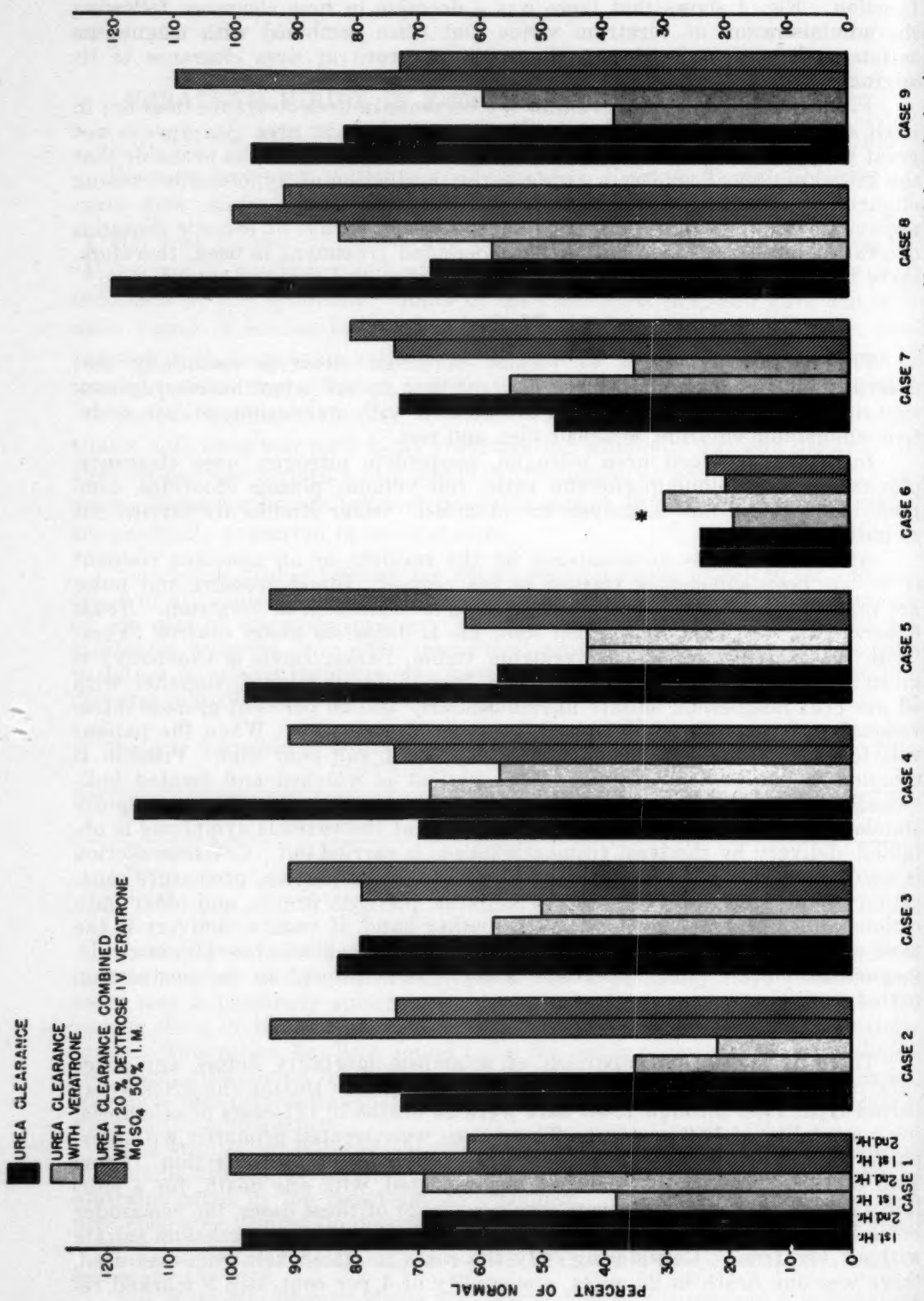
Fig. 1.—Effect on urea clearance produced by Veratrone and Veratrone combined with magnesium sulfate and hypertonic glucose.

Note.—Chart shows the urea clearance studies with Veratrone and also with the combined adjuncts of 20 per cent dextrose in distilled water intravenously and 50 per cent magnesium sulfate intramuscularly. Cases 6 and 7 had severe toxemias of long standing.

*Case 6.—Chronic nephritis with hypertension.

The markedly lowered mortality in the entire 34 cases is thought to be a significant figure even though veratrum was not used in all of them, for it emphasizes the role the drug has played in encouraging conservative treatment and avoiding hasty intervention.

TABLE II. COMPARISON OF MORTALITY IN ECLAMPSIA BEFORE AND AFTER USING VERATRUM VIRIDE

	NO. OF CASES	MATERNAL DEATHS	MORTALITY
Maternity Hospital, University Hospitals of Cleveland			
1930-1945	121	15	12.9%
1945-1950 (Veratrum in 25)	34	1	2.9%
Boston Lying-in (Irving) mortality in the three five-year periods from			
1922-1937	–	–	28.1%, 25.0%, 29.2%
1940-1946, using veratrum	32	2	6.2%
Cincinnati General (Bryant and Fleming)	160	3	1.8%

Table II also shows the excellent result reported by Bryant and Fleming in their large series, and the improvement reported by Irving[7] after veratrum was incorporated into his treatment.

Comment

The results obtained with veratrum viride in our clinic are impressive, especially when pooled with those reported by other investigators. While the drug is not regarded as a cure it does strike at a point early in the vicious cycle of events which are thought to lead to eclampsia, i.e., vasoconstriction. Other successful conservative treatments have been used and reported but none appears to have produced such a consistent improvement in mortality rates as has the veratrum viride regime of Bryant.

Our chief objective is the control of the patient until she can be safely delivered with minimal risk to mother and infant. Veratrum viride, in combination with magnesium sulfate and hypertonic glucose, has so far offered the greatest hope of accomplishing this end.

Summary

1. The fifteen-year incidence of toxemia and eclampsia at Maternity Hospital, University Hospitals of Cleveland, has been presented.

2. The treatment of eclampsia with veratrum viride, magnesium sulfate, and hypertonic glucose has been outlined.

3. Urea clearance studies on nine patients indicate that diminution following veratrum viride is slight and transient and returns to normal levels when combined with magnesium sulfate and hypertonic glucose.

4. A comparison of mortality statistics at Maternity Hospital has been found to be 12.9 per cent before veratrum viride was included in the treatment of eclampsia and 2.9 per cent after its use was begun.

5. It is suggested that the drug is especially valuable in that it makes it possible to control the eclamptic patient until delivery can be safely undertaken.

Fig. 1.—Effect on urea clearance produced by Veratrone and Veratrone combined with magnesium sulfate and hypertonic glucose.
Note.—Chart shows the urea clearance studies with Veratrone and also with the combined adjuncts of 20 per cent dextrose in distilled water intravenously and 50 per cent magnesium sulfate intramuscularly. Cases 6 and 7 had severe toxemias of long standing.
*Case 6.—Chronic nephritis with hypertension.

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Department of Case Reports
New Instruments, Etc.

DECIDUAL POLYPS OF THE CERVIX

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ALTHOUGH cervical polyps have little tendency to undergo malignant change, they are often viewed with suspicion, particularly when showing a rapid increase in size. During pregnancy the physiological changes which occur in the cervix and the added danger of disturbing the pregnancy may make the diagnosis and treatment of these polyps a more difficult and serious problem. In the past five years we have observed four unusual cases of cervical polyps in our outpatient surgical pathology service that will clearly illustrate this.

CASE 1.—Mrs. R. R., a 33-year-old white woman, gravida iii, para i, consulted her physician on June 1, 1948, because she thought she was pregnant. Her last menstrual period prior to this visit was on March 13, 1948. Examination revealed the uterus to be enlarged and soft. The cervix was slightly eroded and a small polypoid tongue of grayish white tissue was noted protruding from the cervical os. The polyp was not removed until a return visit on June 22, 1948, at which time the body of the polyp was grasped with a sponge forceps and gently twisted free from its pedicle. The histology of the lesion was that of a cervical polyp showing decidual reaction. She had no bleeding prior to or after removal of the polyp. The patient delivered, at term, a male infant weighing 10 pounds, 8 ounces, after a 12-hour labor. The infant was manually rotated from a deep transverse arrest position to a right occipitoanterior position, and was delivered by midforceps extraction. The mother was Rh negative, the father was Rh positive, and the child was Rh positive. At her six weeks post partum examination the cervix was normal. Her first pregnancy in 1944 terminated in a spontaneous abortion at three months. In 1946 she had a normal pregnancy delivering without difficulty a male infant weighing 8 pounds, 14 ounces. She had an abdominal operation in 1943 at which time the appendix and three leiomyomas of the uterus were removed.

CASE 2.—Mrs. V. A., a 33-year-old white woman, gravida ii, para i, was first seen on Feb. 10, 1950, because she thought she was pregnant. Her last menstrual period was on Dec. 17, 1949. Upon examination, the uterus was of a size compatible with a six to seven weeks' pregnancy. The anterior lip of the cervix was eroded and there was a grayish white polyp noted in the cervical os. The polyp was removed by the same procedure as used in Case 1. Microscopic examination showed a cervical polyp containing decidual reaction. The patient had a few episodes of light bleeding after the polyp was removed but her pregnancy has progressed satisfactorily. When last examined on June 13, 1950, the cervix showed marked erosion but no polyp formation was present. She had a normal pregnancy approximately two years ago and delivered a male infant weighing 7 pounds, 2 ounces.

CASE 3.—Mrs. E. K., a 27-year-old white woman, gravida ii, para i, had the cervix cauterized several times for a cervical erosion since October, 1949. On April 17, 1950, she returned for an examination of the cervix and her physician noted that the uterus was soft and slightly enlarged. The cervix was also soft and in the cervical os was a large grayish red

polyp. It, likewise, was twisted free from its pedicle with a sponge forceps. Microscopic study showed the lesion to be a cervical polyp containing decidual reaction. The cervix had previously been examined on March 13, 1950, which was one month prior to the discovery of the polyp and no polyp formation was noted at that time. Her last menstrual period was on Feb. 13, 1950. She has had no bleeding during this pregnancy. Her first pregnancy, six years ago, was normal.
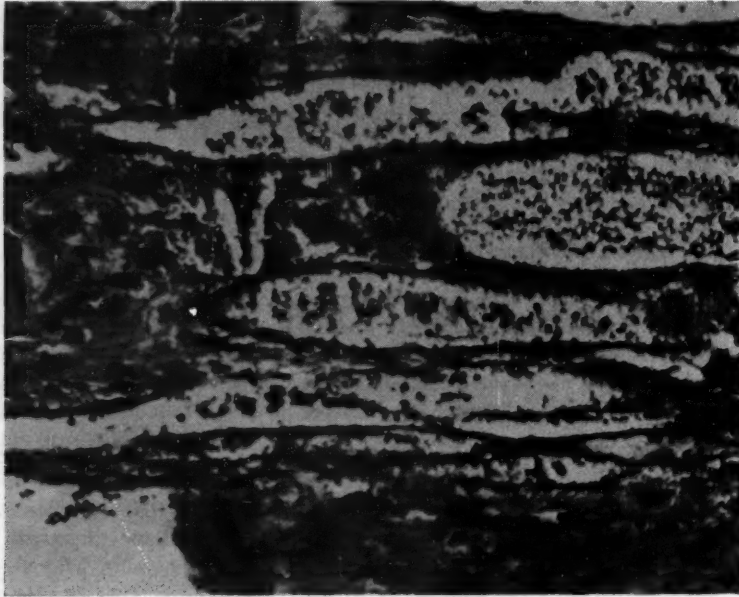

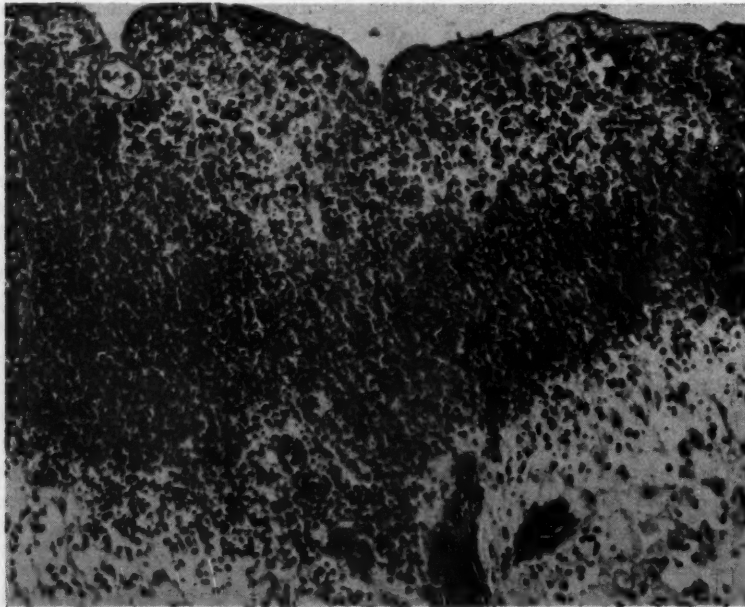Fig. 1 (Case 1).—Necrotic fragment of cervical polyp showing decidual reaction.

Fig. 2. (Case 2).—Section of cervical polyp showing surface ulceration and decidual reaction of edematous cervical stroma.

CASE 4.—Mrs. C. H., a 19-year-old white woman, gravida i, para 0, had a menstrual period on Feb. 17, 1946, which lasted only three days. Her last normal period prior to this was on Jan. 25, 1946. On May 3, 1946, she developed abdominal cramps and vaginal bleeding. The patient consulted two physicians in southern Iowa on May 31, 1946, and was advised to see a specialist in Des Moines because of a suspicious lesion which had been noted on the
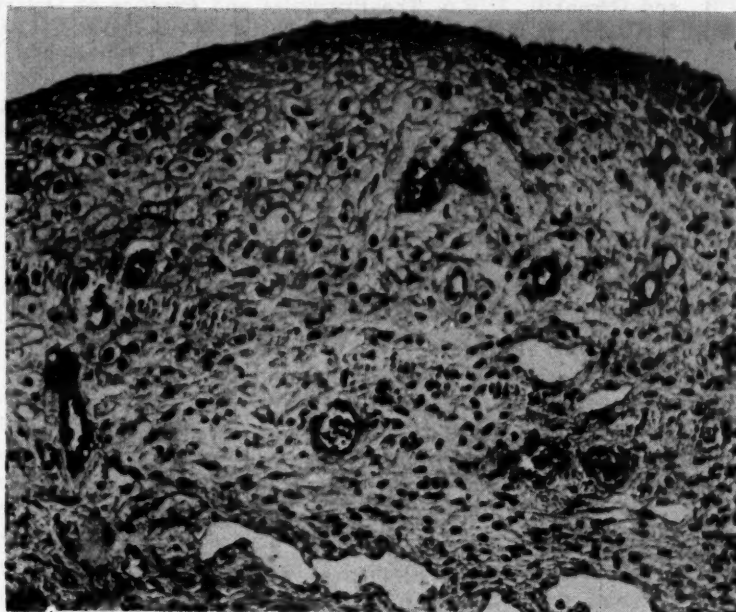

Fig. 3. (Case 3).—Microphotograph of cervical polyp showing decidual reaction beneath surface epithelium.

Fig. 4. (Case 4).—Microphotograph of cervical polyp showing marked decidual reaction of stroma.

cervix. She was first seen in Des Moines on June 17, 1946, and it was estimated the fundus of the uterus extended 25 cm. above the symphysis pubis. At the time of this examination the pregnancy was thought to be of four months' duration.

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CARCINOMA OF THE PANCREAS WITH METASTASIS TO THE CERVIX UTERI*

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METASTATIC cancers of the cervix uteri from extrapelvic sites are rare. In a statistical review of carcinoma of the breast Töröck and Wittelshöfer[1] in 1880 reported 17 cases which had spread to the uterus. They did not divide their cases into those involving the corpus and those affecting the cervix. In 1892 Schaper[2] found a carcinoma of the lung metastasizing to a fundal intramural fibromyoma. He mentioned in his paper that Boisser and Cornil in the *Bulletin de la Société Anatomique* in 1875 submitted a case of an adrenal cancer involving the myometrium of the fundus as two discrete nodules. Von Franque[3] included in his detailed account of carcinoma of the uterus a case of primary carcinoma of the stomach which had metastasized to the cervix. In this same paper are mentioned two reports of secondary uterine carcinoma, one by Metzger and the other by Fränkel, in which the primary sites were the breast and stomach, respectively. In neither of these cases was the cervix mentioned. Charache,[4] in 1941, reviewed the world's literature on metastatic carcinoma of the uterus. At that time he found only 56 cases and then added three of his own. Of the 56, 31 arose in the breast, 14 in the stomach, 3 in the lungs, 2 in the kidney, and one each in the pleura, pancreas, liver, and gall bladder. He made no mention of the exact site of the uterine lesion and gave no specific references pertaining to these cases. We were unable to find the report of the metastasis from the pancreas in the literature; hence we cannot speak more specifically with respect to this reported case. The three cases which he himself reported were primary carcinoma of the breast. Two of them metastasized to the cervix. Finally, Williams, in 1945, described a secondary cervical cancer from a primary carcinoma of the stomach.

We wish to describe another case of this infrequent uterine metastasis, making a total of 60 cases reported in the literature to date as far as we have been able to determine. The primary neoplasm in this instance was a carcinoma of the pancreas. It was unusual not only because of its rarity but also because it was mistaken clinically and pathologically for a primary cancer of the cervix.

The patient was a 65-year-old white woman who was referred to the Gynecological Out-Patient Clinic of the Department of Obstetrics and Gynecology, Jefferson Medical College Hospital, on May 10, 1948, and was subsequently admitted to the Gynecological Ward Service. Her chief complaint at the time was slight vaginal bleeding and dull pain in the lower left quadrant of the abdomen, both of one week's duration.

Her menopause had occurred at the age of 51, and she had had no definite vaginal bleeding until one week before admission. She had noted, however, a slight vaginal discharge which was blood tinged occasionally for two months before the onset of the present symptoms.

She had borne four children vaginally with no complications during the puerperium. She was hospitalized for pulmonary tuberculosis at the age of 30 for an unknown period of time and the disease was apparently completely arrested. She had lost "considerable" weight and had noted anorexia, nausea, and nervousness during the year before admission.

Physical examination revealed slight edema of the ankles and a regular, tender, fixed mass measuring about 14 cm. in diameter in the left hypogastrium. Pelvically there was no evidence of infection of the vulvovaginal glands. The introitus was marital. There was slight relaxation of the anterior and posterior vaginal walls. The cervix was replaced by necrotic neoplastic tissue which destroyed the normal cervical architecture. The growth involved both anterior and posterior vaginal walls to some extent. The fundus was irregularly enlarged to the size of a 3 months' gestation, and was partially mobile; both adnexa were fixed and indurated.

The clinical impression was squamous-cell carcinoma of the cervix, Group IV (Schmitz), Stage 3, League of Nations.

Laboratory Findings.—Red blood cells 4,000,000, hemoglobin 68 per cent, white blood cells 7,900, urine 3+ albumin, urine culture: *B. coli*, blood urea nitrogen 13.6 to 16.4 mg./100 c.c., urea clearance 120 per cent of normal, Wassermann and Kahn tests negative, culture from cervix: *Staphylococcus albus*, diphtheroid bacillus, sedimentation rate: 21 mm. in 10 minutes.
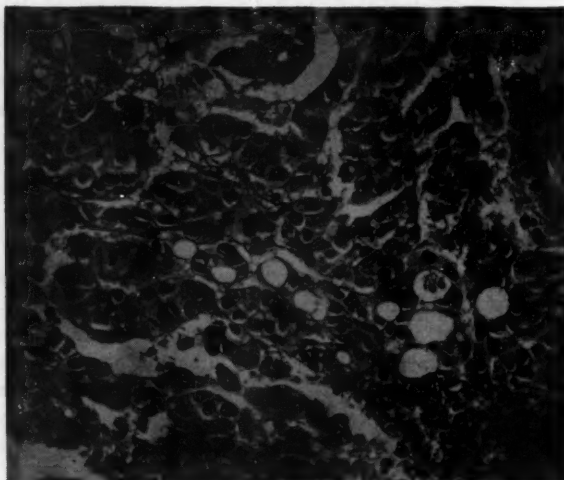

Fig. 1.

X-ray Findings.—Chest, old fibroid tuberculosis; skull, negative; long bones, negative; Intravenous pyelogram, minimal obstructive manifestations in the lower portion of the urinary tract, slightly more pronounced on the left; barium enema, narrowing of the midsigmoid, probably due to a lesion extrinsic to the bowel.

Proctoscopic Examination.—Scope passed 4 inches only. The large irregular mass of the cervix uteri was palpable per rectum. It displaced the anterior rectal wall but was not causing any obstruction. The sigmoidoscope could not be passed further than 4 inches because of the fixed mass which prevented proper maneuvering of the instrument. The mucosa as far as this point was normal.

Biopsy.—The biopsy of the cervical lesion was simply reported as an anaplastic carcinoma of the cervix, high grade (Grade IV) malignancy (Fig. 1).

Clinical Progress.—External irradiation was commenced on May 13, 1948, and amounted in all to 2,450 r units to each of four portals of 10 by 15 cm. size. The factors involved were 200 kv., 25 ma., skin target distance 50 cm., and filtration of 1 mm. copper and 1 mm. aluminum.

The patient was discharged on May 20 to continue external radiation as an outpatient. In June 25, 1948, when examined in the Carcinoma Follow-up Clinic, she was found to be markedly jaundiced and was admitted to the hospital. She was also nauseated and had bowel and bladder discomfort. The jaundice had developed during the previous two weeks.

The hypogastric mass was still present, but the cervical lesion had regressed considerably. The uterus did not seem to be as large as was previously noted but was less mobile. She was given supportive therapy but declined rapidly and died on July 9, 1948.

Postmortem Examination.—An autopsy performed 3½ hours after death revealed the following significant findings:

The vagina was of normal size. The surface epithelium was irregularly congested and somewhat fibrotic but did not show any definite ulceration. The irradiated cervix appeared to have regressed in size, and the canal was patent. Both the external surface and the canal were rough, and the mucosa appeared mottled light gray and red. There was no definite ulceration. The consistency was firm. Cut surfaces disclosed diffuse fibrosis, with deep furrows extending radially from the cervix into the adjacent tissues and parametrium. The endometrial cavity was essentially normal. The myometrium measured 2 to 3 cm. in thickness. It was firm, yellow, and fibrous. The serosa disclosed some light yellow necrotic tissue on its surface. There were no fibroids present, the uterine tubes were normal, and the ovaries somewhat hemorrhagic. The broad ligaments were free except for the portions adjacent to the cervix; these areas were indurated, firm, and yellowish-gray, and contained no discrete nodules. The vesicovaginal and rectovaginal septa were thickened but grossly free of neoplastic tissue. The iliac veins were normal, and grossly the regional lymph nodes were of normal size and consistency.
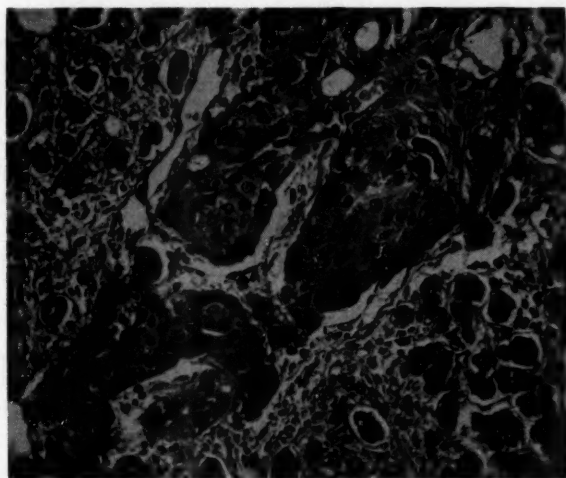

Fig. 2.

Cut surfaces of the left kidney disclosed numerous conglomerate and irregularly outlined tumor nodules that measured as much as 2 cm. in diameter throughout the entire structure, but which were more marked at the superior pole. These nodules were mottled, being yellow-gray and hemorrhagic.

The pancreas was of approximately normal shape and size, and measured 16 cm. in length. The external surface was irregularly lobulated; the posterior surface was densely adherent to the posterior abdominal wall. The head measured approximately 5 cm. in diameter. Both the head and the body were extremely firm and indurated. Cut surfaces likewise disclosed mottled gray and yellow tissue which blended gradually with the surrounding fat.

The common bile duct for a distance of 4 cm. was irregularly and completely occluded by pressure from the adjacent surrounding pancreas. Above this obstruction, the common bile duct was greatly dilated, measuring 5 cm. in its greatest circumference. The lumen was filled with dark green to black bile. The distention of the duct continued upward to involve not only the proximal portion of the intrahepatic bile ducts but also the smaller intrahepatic biliary radicals. The gall bladder was likewise distended. There were no stones. The lymph

nodes along the pancreas, abdominal aorta, liver hilum, and base of the mesentery were enlarged, matted together, and measured as much as 4 cm. in diameter. They were completely replaced with fibrous tissue.

The liver weighed 1,170 grams and measured 25 by 16 by 6 cm. The external surface was smooth, glistening, and mottled light and dark brown. The edges were fairly sharp and the consistency was firm. Cut surfaces disclosed a moderate degree of dilatation of the biliary radicals and a considerable degree of bile staining to render a nutmeg appearance. There were no abscesses or other abnormal foci.

The apices of both lungs showed irregular nodules of old, healed fibrocaseous tuberculosis. There were no active tubercles or areas of cavitation.

Histologically the pancreas showed the presence of irregular cords and nests of cells. Many of the larger masses showed central areas of necrosis and/or hemorrhage. At times there was distinct acinar formation, rendering an appearance similiar to that of the normal pancreatic tissue (Fig. 2). The cells forming this neoplastic tissue were large and polyhedral, had indistinct borders and a pink cytoplasm. They contained large hyperchromatic nuclei usually centrally placed. There was, however, considerable variation in size, shape, and staining of cells and nuclei. Foci of similar cells were seen invading the entire uterus, the cervix, the broad ligaments, both ovaries, both adrenals, and those lymph nodes which were enlarged grossly. The liver was free of metastasis but showed severe degeneration with focal periportal necrosis.

Summary

According to Herbut[6] the most common secondary sites of a carcinoma of the pancreas are in the regional lymph nodes, liver, peritoneum, lungs, gall bladder, diaphragm, mediastinal nodes, and pleura. A case of metastatic cancer of the cervix arising in the pancreas is described. As far as we can ascertain this is the second report of pancreatic carcinoma spreading to the uterus, and we believe it is the first of its kind that definitely involved the cervix. As was shown, the anaplasticity of the tumor led to the incorrect interpretation of primary carcinoma of the cervix. Although metastatic tumors of the cervix are rare, it behooves one to remember that they do exist and that occasionally carcinoma of the cervix may not be a primary lesion.

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BILATERAL OVARIAN DERMOIDS IN PREGNANCY

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THE entity of bilateral ovarian dermoids in pregnancy is sufficiently uncommon to warrant the reporting of an additional case.

In 1940, Andrews and the Nicholls[1] reviewed the literature and reported on 44 cases including their own case. It might be noted that each of these cases was treated by bilateral oophorectomy with or without additional procedures. Since then there has been no review of this entity per se, although Hamilton and Higgins,[2] in 1949, reviewed the subject of ovarian tumors in pregnancy and included a compilation of cases of bilateral dermoids, bringing the total number of reported cases up to 57. Since this review, we have found 8 additional cases.[3]

It was our fortune recently to see a case of bilateral dermoids in pregnancy. This case, as described below, was treated at term by cesarean section and conservative ovarian surgery.

The patient, E. O., a 27-year-old, para 0, gravida 1, was first seen in our Ante-Partum Clinic on March 23, 1949. Her last menstrual period was Dec. 5, 1948, and expected date of confinement computed to be Sept. 12, 1949. History and physical examination at this time revealed a 60-inch white woman whose weight was 169 pounds (normal weight 168 pounds) who was approximately 3 to 3½ months pregnant, with no detected abnormalities. Antepartum course was uneventful until routine vaginal examination 6 weeks prior to term revealed a large cystic mass which was not movable and appeared to arise from the left adnexa. It was felt that the mass would not allow a vaginal delivery. X-ray of the abdomen at this time revealed the presence of the pregnancy and a calcified structure resembling a tooth in the left adnexal region (Fig. 1). The patient was admitted to the hospital on Sept. 2, 1949, for elective cesarean section. Examination at this time revealed that the cervix was dilated 2 cm., and the vertex was presenting well up in the pelvis. A firm mass was felt in the cul-de-sac displacing the cervix and fetal head up and to the right; the mass seemed to be fixed, the baby was judged to be large, and therefore cesarean section and ovarian surgery were decided upon as the preferred treatment. On Sept. 3, 1949, under spinal anesthesia, a laparotrachelotomy was performed and a 9 pound, 13 ounce male was delivered. After closure and reperitonization of the uterus, two cysts were found posterior to the uterus: the one on the left, measuring 12 by 7 cm., completely replaced the ovary, the one on the right measured 4 by 5 by 3 cm. A left oophorectomy and right ovarian cystectomy were performed with preservation of almost all of the right ovarian substance, the cyst being easily shelled out.

Pathological Report.—Diagnosis, bilateral dermoid (cystic teratoma). They showed the characteristic picture, each being lined by squamous epithelium supported by a corium which included many sebaceous and sweat glands and hair follicles. Cartilage and bone tissue were also present. The cysts were lined with cheesy, fatty material and hairs.

The postoperative course was uneventful and the patient was discharged on the tenth postoperative day. The patient has been followed in postpartum clinic. Her menstrual function has been normal. On March 27, 1950, endometrial biopsy on the twenty-fourth day of the cycle revealed secretory endometrium (Fig. 2).

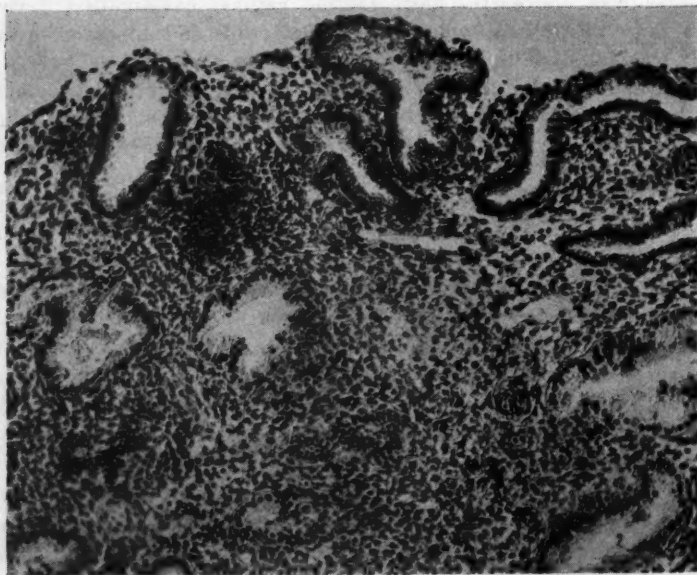Fig. 1.—X-ray of abdomen revealing calcific structure in left adnexal region.

Fig. 2.—Endometrial biopsy on twenty-fourth day of cycle revealing secretory characteristics.

Comment

It is very regrettable to state that out of a total of 66 reported cases of bilateral ovarian dermoids in pregnancy (including this report) only 10 cases were treated conservatively with preservation of ovarian tissue. It must be admitted that there must have been some functioning ovarian tissue present to have allowed the pregnancy to occur and that, therefore, there must have been some ovarian tissue to be conserved at the time of operation. (In only a very few cases can we assume that the further growth of the cyst during the course of the pregnancy so obliterated the remaining ovarian tissue as to render a conservative operation impossible.) It is our feeling that conservative ovarian surgery is very much indicated in this group of cases.

Summary

1. An additional case of bilateral ovarian dermoids in pregnancy is reported, bringing the total number of reported cases up to 66.

2. Of the total number of cases reported only 10 cases were treated with conservative ovarian surgery.

3. The present patient treated conservatively has continued to menstruate normally and endometrial biopsy done 6 months post operation revealed secretory endometrium and thereby gives presumptive evidence of ovulation.

4. A plea is made for conservative ovarian surgery and reasons are advanced to support this plea.

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CHORIONEPITHELIOMA OF UTERUS ASSOCIATED WITH TEMPORARILY NEGATIVE BIOLOGIC TESTS FOR CHORIONIC GONADOTROPIC HORMONES

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CHORIONEPITHELIOMA is a neoplasm that is characteristically associated with positive tests for chorionic gonadotropic hormones. Most case reports and textbooks concerned with this subject state that the tumor is "usually" or "invariably" or "consistently" associated with such positive tests.[1, 2, 3, 13] Mathieu[1, 2] and Mathieu and Palmer[3] have stated, "It is impossible to conceive of a negative Aschheim-Zondek test in the presence of chorionepithelioma"; "the existence of a nidus too small to produce a positive pregnancy test is a rarity and probably explains those few cases reported in which there was a negative pregnancy test. . . ." In the minds of both clinicians and pathologists, a dependence has been built up on the association of positive tests with chorionepithelioma so that when a negative test is found, confidence in the validity of the biologic tests or the histological diagnosis is shaken. The following case report exemplifies this course of events.

F. B., a 23-year-old Caucasian housewife, was admitted to Centinela Hospital on April 24, 1949, complaining of vaginal bleeding at irregular intervals which had been rather heavy in the past two weeks. Her only known pregnancy resulted in a normal full-term delivery on April 27th, 1948. The placenta was expressed spontaneously and appeared complete. Both mother and child were discharged on the fifth hospital day without incident. Postpartum examination at the sixth week showed satisfactory involution of the uterus.

Menstrual periods were normal every thirty days until Oct. 16, 1948, when the flow lasted for fourteen days. The period on November 16 was normal, but slight spotting followed. The December and January menstrual periods were normal but the February period was heavy and lasted seventeen days. After an interval of four days and until her admission to the hospital on April 24, 1949, vaginal bleeding was irregular and heavy.

Physical examination at that time revealed no significant findings except slight bogginess of the uterus and bleeding through the cervix. Blood count and urinalysis were noncontributory. A diagnostic dilatation and curettage of the uterus were productive of a fairly large amount of tissue. Histological examination of this material (to be discussed in more detail below) revealed a pleomorphic malignant tumor and a panhysterectomy with bilateral salpingo-oophorectomy was done on April 29, 1949. At the time of surgery, no evidence of tumor extension was found.

The patient's recovery from surgery was uneventful and she was discharged from the hospital on the seventh postoperative day. She was then referred to Dr. Ian MacDonald for radiation therapy. During the course of the therapy, a metastatic tumor nodule appeared in the right mandibular region, which, on needle biopsy, proved to be similar to that found in the uterus. Despite active and supportive therapy, the patient's condition progressively deteriorated. She was re-admitted to Centinela Hospital on July 25, 1949, appearing acutely ill and emaciated. The abdomen was distended with fluid. An x-ray film of the chest revealed numerous areas of increased density suggestive of metastatic tumor nodules. The patient's condition was critical, and she died on July 31, 1949. Permission for a post-mortem examination was denied.

Pathology.—Report of the curetted material submitted for examination on April 24 consisted of a moderately large number of irregular pieces of tissue varying from several millimeters to 2 cm. in greatest diameter. Microscopic examination revealed some normal endometrium, and considerable tumor tissue. The latter was composed of undifferentiated masses of tumor cells which were large, pleomorphic, containing abundant granular, acidophilic cytoplasm. The nuclei were large, hyperchromatic, and varied considerably in size, and many mitotic figures were present. Part of the tumor tissue was necrotic with superimposed inflammatory reaction. The initial diagnosis was "pleomorphic carcinoma, probably chorionepithelioma."
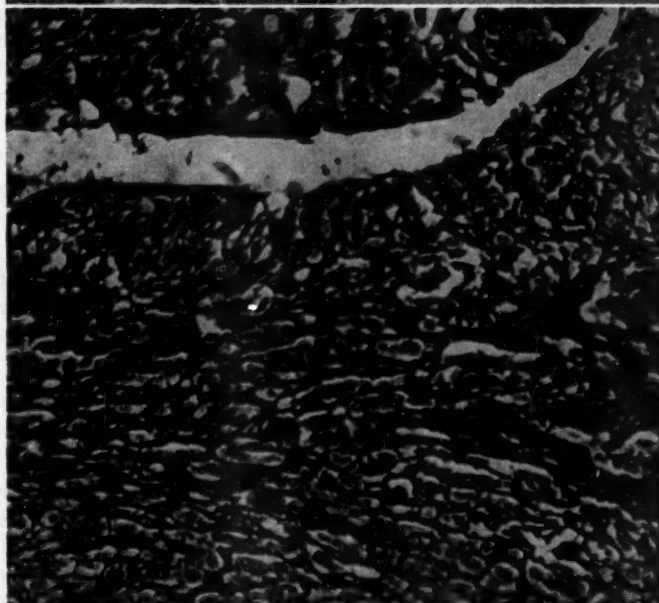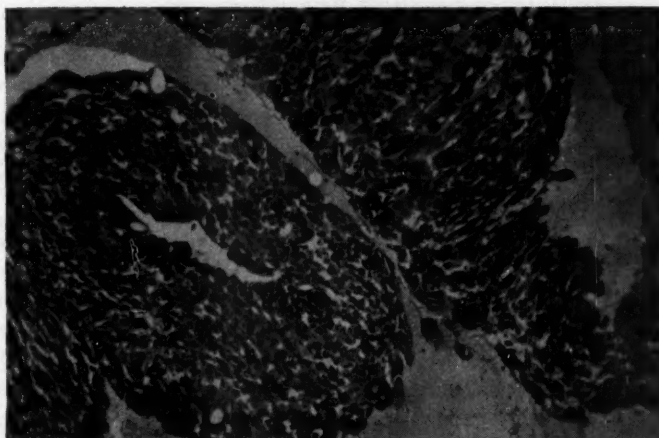
Fig. 1.

Fig. 2.

Fig. 1.—Chorionepithelioma of the uterus with invasion of maternal blood sinus. (H. and E. stain.)

Fig. 2.—Chorionepithelioma of the uterus. (Wilder's reticulum stain.)

The specimen submitted on April 29 revealed no significant gross or microscopic abnormality of the ovaries, uterine tubes, or cervix. The uterus weighed 163 grams. In the fundus was a coarse-textured hemorrhagic tumor mass 4.5 cm. in diameter, which penetrated the myometrium for a distance of 1.9 cm. The line of demarcation between tumor and

myometrium was fairly sharp. The uninvolved myometrium felt boggy and measured 3 cm. in maximum thickness. Sections of the tumor presented a pattern identical to that described in the curetted material. In addition, there were numerous large endothelium-lined channels similar to those seen in a pregnant uterus. These channels were surrounded and invaded by the tumor cells (Fig. 1). Sections of this tissue stained for reticulum by Wilder's technique revealed abundant reticulum surrounding most of the tumor cells (Fig. 2). Elastic tissue and azocarmine stains were noncontributory. The myometrium regional to the tumor presented prominent vascular structures and hypertrophy of the muscle fibers. There was moderate pathological hyperplasia of the regional endometrium. The final diagnosis was "chorionepithelioma of the uterus."

Comment.—One Friedman test and two frog tests (using the *Rana pipiens*) were done consecutively on the patient's urine just prior to hysterectomy. The specimens were nontoxic and of adequate specific gravity. The hormones from 100 c.c. of urine were absorbed and concentrated by the kaolin technique for injection into the frogs. All tests were negative. The results caused us to doubt the histological diagnosis of the chorionepithelioma and the doubt was further supported by the knowledge that the only pregnancy preceding the tumor was a normal one a year previously.

In attempting to exclude the diagnosis of chorionepithelioma, we were left with the possibilities of endometrial carcinoma, endometrial sarcoma, and malignant deciduoma. Of these, we favored the last named, primarily because the histological pattern of the lesion, chiefly the dilated vascular sinuses, seemed to relate the tumor to origin during pregnancy. Reference to the textbooks was confusing, but careful reviews[4, 5, 6, 7, 11] revealed that Sanger (1889) first proposed the term "deciduoma malignum," and later Williams (1895) again used the term "deciduoma," that these authors had reference to a tumor originating from the chorionic villi and not truly from decidua and, therefore, were speaking of chorionepitheliomas. We have been unable to find reference to a true neoplasm of decidua. Ewing[4] quotes Ruge and Meyer, who, in classification of endometrial sarcoma, describe one variety as sarcoma with "decidua-like cells" but these are not associated with pregnancy, and may represent "transitory effects of the menstrual influence."

The slides of the tumor were shown to one group of pathologists, all of whom, influenced by the negative biologic tests for chorionic gonadotropic hormones, rejected the possibility of chorionepithelioma and suggested the probability of endometrial sarcoma, decidual variety.*

While the final diagnosis hung in the balance, the patient was admitted to the Centinela Hospital in a terminal condition. A repeat Friedman test at this time was strongly positive, in view of which everyone concerned conceded the accuracy of the diagnosis of chorionepithelioma.

That the tumor developed following a normal pregnancy need not have been of great concern since about 20 per cent of the cases reported[5] followed normal pregnancy while 45 per cent followed hydatidiform moles, and 35 per cent followed a history of abortion.

While most of the emphasis in the literature is placed on the constancy of positive biologic tests for chorionic gonadotropic hormones in association with chorionepithelioma and also on the relatively high titers of these hormones,[10] isolated reports and comments also appear[5, 7, 8, 9, 12, 14] regarding the occurrence of negative tests with chorionepithelioma. These are regarded by some[1, 2] as errors in technique, a phase in transition from normal to malignant tissue, or insufficient tumor tissue to produce significant amounts of the hormone.

The last two explanations hardly apply to our case because the tumor was large. Since the test was performed three times by two different methods and all steps were entirely satisfactory, it is unlikely that the technique was faulty. We are faced, therefore, with the following additional possible explanations: (a) that the tumor failed to produce a signifi-

*These slides were also sent to Dr. A. T. Hertig who made an objective diagnosis of chorionepithelioma to which he adhered despite the knowledge of the negative biologic tests.

cant amount of hormone, despite its mass; (b) an inhibitory substance was temporarily elaborated which interfered with the biologic tests; or (c) the hormone was rapidly destroyed, so that the amount excreted was small.

It must be accepted, despite the absence of a satisfactory explanation, that negative biologic tests for chorionic gonadotropic hormones may be found in association with chorionepithelioma, that such evidence must not influence the diagnosis, and that more reliance must be placed on the objective histological examination of the tumor tissue. Furthermore, despite initial negative biologic tests, repeated tests at regular intervals may be valuable for therapeutic, prognostic, and diagnostic purposes should the tests suddenly become positive.

Summary and Conclusion

A patient with chorionepithelioma developing one year following a normal delivery is presented.

Initital Friedman and frog tests (*Rana pipiens* using concentration technique) were negative. A repeat test late in the course of the disease became strongly positive.

The cause of the initial negative tests is unknown, but may be due to a temporary failure of the tumor to secrete the hormones, a temporary inhibition of the hormone activity by some other naturally occurring substance in the body, or active destruction of the hormone.

More reliance should be placed on the objective histologic study of the tumor tissue.

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CHORIONEPITHELIOMA

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FORTUNATELY, chorionepithelioma or choriocarcinoma, does not occur often. It may follow hydatid mole or abortion, or rarely a full-term pregnancy. It is a highly malignant tumor. The number of such cases seen by most clinicians is certainly very limited. For this reason, reviewing the problems of others on the subject should help one to keep this possibility in mind in all cases of postpartum bleeding, whether the amount of bleeding be small or excessive.

A case of chorionepithelioma seen recently at the Medical College of Virginia Hospitals has several unusual and interesting features and seems worthy of presenting for discussion.

This 31-year-old, white, gravida ii, para i, was admitted to the Hospital on Sept. 22, 1948, with a uterine pregnancy, at term, in early labor. Her prenatal course had been uneventful. She was delivered on the day of admission, with low outlet forceps, after an easy labor of 2½ hours. The baby, a full-term living female, weighed 7 pounds, 6 ounces, and seemed in good condition. The placenta separated spontaneously and was easily expressed. The blood loss was not in excess of 150 c.c. The placenta was grossly normal.

The lochia rubra checked up on the third or fourth day post partum and there was no further bleeding until sixteen days post partum, six days after leaving the hospital, when she started bleeding excessively from the vagina. She was in profound shock when re-admitted. After she received 1,000 c.c. of blood, her condition permitted curettage and uterine packing, which controlled the bleeding. Another transfusion of 500 c.c. of blood was given after the curettage. Examination revealed the uterus enlarged to the size of a grapefruit and boggy. The cervix was dilated to admit one finger easily. A moderate amount of tissue was curetted from the uterus.

The uterine packing was removed after eighteen hours and there was excessive bleeding from the uterus immediately. Approximately 500 c.c. of blood were lost before it could be controlled. The uterus was again curetted and packed but bleeding continued through the packing. A supracervical hysterectomy was necessary to control the bleeding. One thousand five hundred c.c. of blood were given during the procedure.

Microscopic and macroscopic examinations of the uterus failed to reveal any unusual lesion. The uterus was enlarged and boggy. The day after the hysterectomy was done, a report of the microscopic examination of the first curettings stated that "sections of the endometrial scrapings exhibit several areas in which there are sheets of proliferating trophoblasts." The pathologist did not feel that the sections justified the diagnosis of choriocarcinoma.

Five weeks after the hysterectomy, two months post partum, she started bleeding excessively from the bladder. Cystoscopy, by Dr. A. I. Dodson, revealed a soft, hemorrhagic mass in the region of the bladder trigone. A biopsy showed chronic inflammation. A positive diagnosis of chorionepithelioma was not made until a second biopsy of the bladder lesion was taken, four weeks after the initial hemorrhage from the bladder, showing the true nature of the lesion. There were three episodes of excessive hemorrhage from the bladder. The blood loss with each was 500 c.c. or more. Blood loss was replaced with repeated transfusions of whole blood. The bleeding was stopped temporarily on each occasion by fulguration of the bladder lesion.

On Dec. 29, 1948, five weeks after the first bladder hemorrhage, and ten days after the positive biopsy, a segmental resection of the bladder was done by Dr. Dodson, with removal of the bladder trigone (site of lesion), cervix, and a portion of the vagina as a block. The ureters were reimplanted into the reconstructed bladder. This procedure was done, first, to control the hemorrhage and, second, with the faint hope that we might be dealing with an isolated metastasis.

Micoscopic examination of the surgical specimen revealed "chorionepithelioma invading the cervical stump and base of the bladder. The tumor cells were seen in the lumen and wall of some of the larger veins."

On Dec. 26, 1948, three days prior to the bladder resection, x-ray of the chest had revealed a density of approximately 3 cm. in diameter in the apex of the right lung which was thought to be an old tuberculous lesion but possibility of metastasis was considered. A series of x-ray films of the chest over a period of three weeks revealed that the lesion was definitely getting larger. During this period of time, x-ray therapy was being given over the pelvis, a total of 4,500 r given through multiple portals.

After considerable discussion and debate in the hospital staff conference, it was agreed that a pneumonectomy should be done as soon as her condition permitted it, in the hope that the metastatic lung lesion was a solitary lesion in the upper lobe of the right lung. Such a case was successfully treated by lobectomy by Dr. Herbert Maier and Dr. Howard C. Taylor[1] at Memorial Hospital in New York in 1943. A pneumonectomy was done by Dr. I. A. Bigger on Feb. 10, 1949. At the time of operation, a considerable number of smaller lesions were found through the lung and pleura which had not shown on x-ray. Pathological examination confirmed the diagnosis of metastatic choriocarcinoma in the lung.

Friedman tests two days and two weeks after pneumonectomy were positive in dilution of 1:10 but negative in dilution of 1:100. X-ray of chest two weeks postoperatively revealed metastatic lesions in the left lung.

Her subsequent course was downhill and she died on May 28, 1949, eight months after delivery.

Autopsy revealed metastases to the remaining left lung but nothing else of importance. There were numerous nodules in the left lung, the largest 8 by 6 cm. The hilar lymph nodes were not enlarged.

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HEMORRHAGIC HYDATIDIFORM MOLE WITH A TWISTED OVARIAN CYST*

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(From the Department of Obstetrics and Gynecology, University of Illinois and the Cook County Hospital)

THE patient, a 27-year-old white woman, entered the Cook County Hospital late in the evening of Jan. 19, 1950. She complained of (1) irregular menses during the preceding year, (2) marked abdominal swelling for the previous 3½ weeks, (3) vaginal bleeding for two weeks, and (4) episodes of sharp lower abdominal pain four days previous to admission which recurred, and was more constant, however, within the last twenty-four hours.

She was a para iv, gravida v, having had a spontaneous abortion in 1944. Her youngest child was two years of age. Normally her menses occurred every 30 to 32 days with a 4 to 5 day flow. During the previous year, however, she noted irregularity in the cycle of her menses varying from 14 to 42 days with a usual 4 to 5 day duration of flow. Dysmenorrhea accompanied this irregularity. Her last menstrual period was in November, 1949. She had no menses in December, 1949. On Jan. 5, 1950, the patient began to bleed vaginally and pass clots. This continued daily with variation in the amount of bleeding up to the time of her admission.

The patient had scarlet fever in 1938 with a residual nephritis and edema. She stated she had edema, pyelitis, and albumin in the urine with several of her pregnancies.

Physical examination revealed the blood pressure to be 134/60, pulse 98, respirations, 20, and temperature 100° F. The breasts were not tender or full, and no colostrum could be expressed. The abdomen was symmetrically enlarged by a mass extending two fingerbreadths above the umbilicus. The mass was slightly movable, exquisitely tender to touch, especially at its most superior portion and laterally. It possessed a doughy firmness in consistency. No fluid wave was detectable. Bowel sounds were normal to slightly diminished. A souffle was heard with a fetoscope over the right lower quadrant but no fetal heart tones were heard. Pelvic examination revealed the vagina to contain free blood and clots. The cervix was hypertrophic, soft, and patulous. The external os admitted a finger with ease but the internal os was closed. The corpus was thought to be the size of a six months' pregnancy or else normal in size with a mass of such a size resting upon it. No round ligaments were palpable. Speculum examination revealed the cervix to be tinged bluish in color.

The following morning the patient was re-examined. A slight increase in the size of the abdominal mass was noted. A diagnosis of a twisted ovarian cyst or hydatidiform mole was made, with a missed abortion or abdominal pregnancy to be ruled out. A blood count revealed a red cell count of 2,640,000 and a white cell count of 11,600. A roentgenogram of the abdomen and pelvis revealed a homogeneous mass occupying the pelvis and part of the abdomen. No fetal parts were discernible. Five minims of Pitocin were injected subcutaneously into the patient's arm. Recurrent cyclic firmness of the mass was detected at 3-minute intervals alternating with periods of less firmness. A laporotomy was performed the following morning. At operation the uterus was found to be mottled, dusky, purplish-pink in color, similar to a Couvelaire uterus, and doughy soft in consistency. The ovaries were enlarged to the size of oranges; they were cystic and lobulated. The left ovary was twisted on its pedicle. As the left adnexa were being clamped for removal, trauma to the lateral wall of the uterus occurred with profuse bleeding. Hemostasis was

achieved with difficulty as each forceps caused further trauma to the friable, mushy uterine
wall. A supracervical hysterectomy, left salpingo-oopherectomy, right salpingectomy, and
partial resection of the right ovary were performed. The uterus was opened and a hydatidi-
form mole with marked intrauterine hemorrhage was found. The patient made an unevent-
ful recovery and was discharged on the eleventh postoperative day.

The pathologist's report confirmed the diagnosis of an intrauterine, hemorrhagic
hydatidiform mole with bilateral follicular cystic ovaries.

The Friedman modification of the Aschheim-Zondek test was positive on the patient's
second and sixth postoperative day.

Thus we have a 27-year-old, para iv, gravida v, with a history of glomerulonephritis
following scarlet fever and possible episodes of nephritic toxemia with her pregnancies,
whose youngest child is 2 years old, entering the hospital with complaints of irregular
menses for one year, rapid enlargement of the abdomen for 3½ weeks prior to admission,
vaginal bleeding for two weeks, and occasional bouts of severe lower abdominal pain. A
limited differential diagnosis led to two possible conditions. Laparotomy revealed both
conditions to be present. The patient made an uneventful recovery. Further follow-up
on the forty-fourth postoperative day revealed an A-Z test to be negative and roentgeno-
grams of the chest, spine, and pelvis to be negative for metastatic involvement.

55 EAST WASHINGTON BOULEVARD.

A NEW RETRACTOR

LOUIS DROSIN, M.D., NEW YORK, N. Y.

THE majority of operators employ self-retaining abdominal retractors and find them efficient in most cases. Many prefer separate retractors, particularly when they have sufficient assistance. In deep-seated or difficult operative fields individual and wide retractors are often imperative. In order to avoid frequent changes in size and to save time and often, also, the irritation of being handed the wrong size, I have devised an adjustable retractor which combines the qualities of dilatation and contraction while the instrument is in situ in the
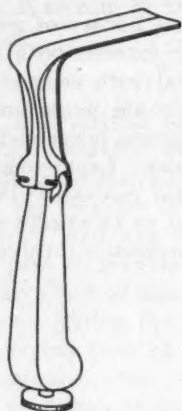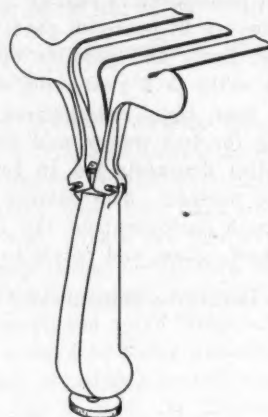
Fig. 1.   Fig. 2.

Fig. 1.—Instrument closed and without the winged flanges on the blades as shown on Figs. 2 and 3.
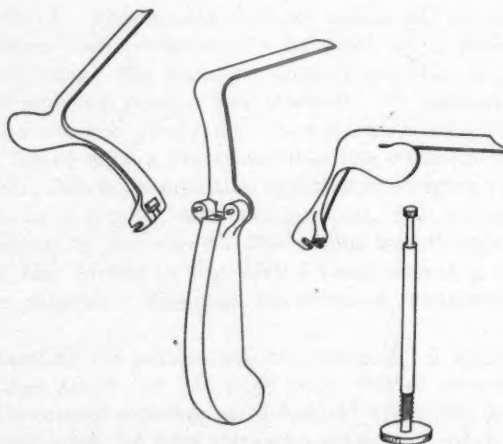Fig. 2.—Shows instrument in widest expansion.

Fig. 3.—Showing the separate parts of the instrument. The handle can be made hollow so as to facilitate cleansing and sterilizing.

operative field. It can easily be taken apart and is readily reassembled. It consists of a middle stationary blade continuous with the handle and two movable blades superimposed on the fixed one. The movable blades are adjustable to the proper amount of dilation or contraction according to requirement, by means of a screw situated at the lower end of the handle. One can thus adjust the blades to any desired width by turning the screw one way or the other. It is equally useful in abdominal as well as vaginal operations.

302 WEST 86TH STREET

A NEW FETOSCOPE*

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(From the Department of Obstetrics, Robert B. Green Memorial Hospital)

ALTHOUGH primarily designed as a fetoscope, this instrument adds greatly to the clarity of breath and heart sounds, thus making it of value to internists as well as to obstetricians. It is compact in design so that it may be worn comfortably around the neck. For ordinary use, the rubber inserts in the side handles serve to cut down extraneous noises. When
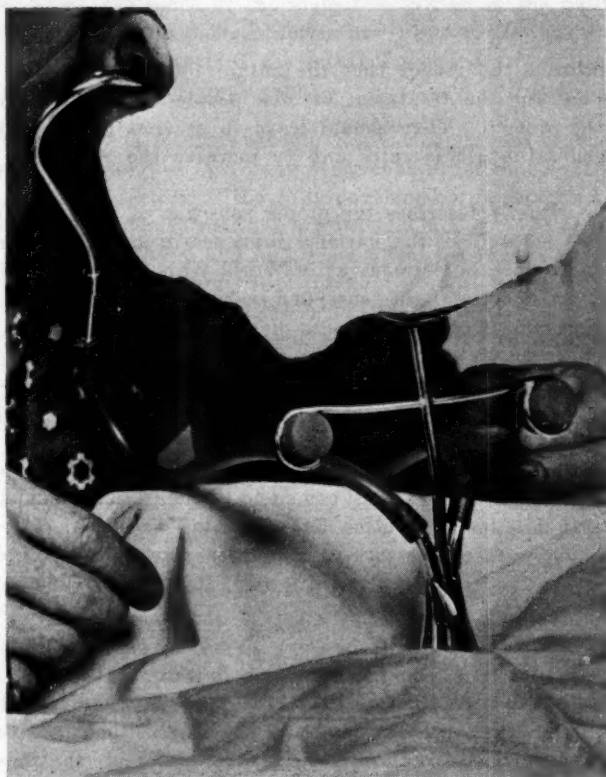

Fig. 1.

the sounds are distant, pressing the forehead against the head piece adds bone conduction to the usual auditory perception and greatly increases total hearing ability. The instrument also has the advantage of not requiring a cumbersome headband to be placed over or around the head. It will fit into a coat pocket and so is quite adaptable to general use.

Department of Book Reviews

EDITED BY PHILIP F. WILLIAMS, M.D., PHILADELPHIA, PA.

Review of New Books

The preface informs the reader that the author intends with this book[1] to use his medical knowledge not for the treatment of sick people but for the enlightenment and instruction of healthy women. They should learn to prevent illness as much as possible by following the general hygienic rules and to increase the resistance of the body by routine gymnastics.

The chapter on hygiene describes the proper selection of food and the importance of vitamins and minerals as well as the harmful influence of undernourishment which very frequently caused amenorrhea in Germany after World Wars I and II. The proper clothing, the influence of heat, the effect of light-, sun-, and seabathing are discussed in detail; general hygienic rules which should be observed during menstruation and after childbirth are given and early postpartum exercises starting on the second day after delivery are shown in six instructive photos. After a historical review about the body culture of women, the author describes the modern training methods for the female body, directed by the anatomy and the specific function of the female sex organs. Each system of the body is analyzed and the favorable influence of routine gymnastics is pointed out. This book may be well recommended to every woman who has full command of the German language and is willing to spend daily several minutes on routine body training at home. The very instructive pictures will encourage the reader to try the thirty-nine exercises but, indeed, it will take some time and effort for the average housewife until the desired effect is reached.

ROBERT TAUBER.

The major portion of this book[2] is devoted to the treatment of thromboangiitis obliterans and arteriosclerosis obliterans. In recent years, there has been an unusual amount of interest in new vasodilator drugs and surgical methods of treating these conditions. The author performs a real service in re-emphasizing the importance of local management of the lesions in the extremities of individuals with occluded arteries. The proper local treatment of gangrenous lesions is often more important in preventing amputation than are all of the other measures. Other arterial diseases discussed more briefly include Raynaud's Disease, erythromelalgia, frostbite, scalenus anticus syndrome, and aneurysms of peripheral arteries.

MEYER NAIDE.

The Breast[3] is a small volume devoted to a consideration of breast diseases and abnormalities and their management. Normal structure and function are considered in the early chapters as a basis for understanding the care of the organ in a pathological state.

[1]**Hygiene und Koerperschulung der Frau.** By Prof. Dr. F. A. Wahl, Cologne, Germany. Pp. 166 with 62 illustrations. Stuttgart, 1950, Georg Thieme. German Marks 16.80.
[2]**Management of Peripheral Arterial Diseases.** By Saul S. Samuels, A.M., M.D., Chief of the Department of Arterial Diseases, Stuyvesant Polyclinic Hospital, New York. Pp. 345 with 112 illustrations. New York, 1950, Oxford University Press. $7.50.
[3]**The Breast.** By F. D. Saner, M.B., B.Ch., F.R.C.S. (Eng.), Surgeon, Royal Northern Hospital. Pp. 316 pages with 193 illustrations and 15 color plates. Baltimore, 1950, The Williams and Wilkins Company. $8.50.

Fourteen individuals collaborate with the author in their respective fields from anatomy to plastic surgery. The contributors, for the most part, convey their personal experience and opinion without undue reference to other sources. I like the physical makeup of the book, its easy readability, its personal touch, and its fine illustrations. The photomicrographs are especially commendable.

This book should find its greatest usefulness for the student, general practitioner, or internist who desires an available reference without great detail. By way of criticism, I believe it lacks balance in some sections since individuals are likely to be overenthusiastic in their given field to the detriment of the volume as a whole. For example, nearly 50 pages are devoted to roentgen therapy and much of this to general radiation physics and techinque. Even the reference to the use of radiation in breast cancer is probably greatly overemphasized, in view of growing experience and sound statistical evaluation of results.

On the other hand, the place of the endocrine system in the palliative treatment of breast malignancy is given only meager notice and little of the latest information.

The section on the importance of the internal mammary lymph nodes in breast carcinoma is particularly timely and significant.   LLOYD W. STEVENS.

We teach embryology in medical schools to give the student a general appreciation of the origins of the separate organs and organ systems in order that he may better appreciate the normal and abnormal function of the fully developed organism, and that he may understand how certain types of malformations are brought about. We have a tendency to use as text material the most detailed and highly technical books on the subject and too often the student who needs only general background information and who will never be a specialist in the field becomes lost in the welter of details.

We might do well to make available in all fields more books like this one written by Dr. Nair that cover briefly and clearly fundamental areas with which a student must be familiar but in which he does not intend or need to be a specialist.

The embryology[4] prepared by Dr. Nair for medical students in India is clear, succinct, and follows current concepts of developmental processes. It does not enter into discussion of controversial minutiae and presents the entire subject in a brief, well-selected form.
                                                                         EDITH L. POTTER

The author of this excellent publication, **Pharmacological Basis of Penicillin Therapy**,[5] has played a primary role in the advancement of knowledge pertaining to the basic pharmacology of penicillin with which this volume deals. In the first part of the book, he concisely summarizes the pertinent facts dealing with the absorption, distribution, inactivation, and mode of action of penicillin. Also, the development and usage of repository forms of penicillin are discussed. The author uses these facts as a basis for a discussion of the various forms and dose schedules of penicillin.

The latter part of the book deals with the renal elimination of penicillin and measures that have been developed to suppress reversibly its tubular secretion. In a new approach to penicillin therapy, the author integrates the fields of renal physiology and enzymology. The application of these principles by Dr. Beyer and his associates led to the development of carinamide and, more recently, to a new compound, Benemid. Unfortunately, very little data regarding the latter drug are contained in this edition of the book, as, from preliminary observations, the coadministration of Benemid with penicillin administered by mouth may well have a marked effect upon the future usage of oral penicillin. This book is a valuable addition to the subject of chemotherapy and is obviously the most thorough and fundamental treatise on the renal elimination of penicillin yet published. It can be used profitably by practicing physicians, research workers, and medical students.   HARRISON FITZGERALD FLIPPIN.

[4] **Human Embryology for Medical Students.** By S. R. Nair, Bombay, India, 1950, The Popular Book Depot.

[5] **Pharmacological Basis of Penicillin Therapy.** By Karl H. Beyer, Ph.D., M.D., F.A.C.P., Director of Pharmucological Research, The Medical Research Division, Sharp and Dohme, Inc., Glenolden, Pa. Pp. 224 with 37 illustrations. Springfield, Ill., 1950, Charles C Thomas. $4.50.

Designed as a monograph, **Primary Carcinoma of the Vagina,**[6] an exhaustive statistical analysis, becomes an account of the experience of the Memorial Hospital in the care of 110 cases of carcinoma of the vagina. Carcinoma of the vagina is a relatively rare form of genital malignancy. The report of the experience with such a large series is therefore of value. Though the possibility of lymphatic spread from the primary source is considered, the conclusions are not based on histological confirmation. The extent of the primary disease with possible locations within the vagina are well outlined. Beyond the local lesion the evidence for spread to regional node represents assumption. This is reflected in the results of therapy and consideration of future treatment in relation to past experience. While radical removal of all areas involved by carcinoma is advocated as the treatment of choice, for the future no observations can be made as to the extent of the surgery necessary to improve the results over the 10.9 per cent five-year survival obtained from radiation used either alone or in combination with surgery.

An extremely thorough statistical analysis is presented on the basis of the study of the records of 110 consecutive patients admitted to the Memorial Hospital between December, 1935, and January, 1946. Unfortunately the material is exactly what it says it is, a review of experience, but falls far short of being a monograph on the subject of primary carcinoma of the vagina.   LANGDON PARSONS.

The second volume of **Progress in Gynecology**[7] is, like the first, a collection of reports on various phases of gynecologic diagnosis and technique. The contributors include many of the outstanding gynecologists of this country and a few from England and Europe, each presenting a subject in which he is particularly interested. This sometimes makes for undue emphasis on relatively unimportant material but in general adds to the effectiveness of the publication. It is hoped that the enthusiasm of some of the authors for unusual procedures, for instance, hysterography in the diagnosis of endometrial carcinoma and retained placenta, will not be contagious.

The presentations are divided into ten major groups: (1) Growth and Physiology, (2) Diagnostic Methods, (3) Functional Disorders, (4) Interrelationship of Endocrine Glands, (5) Sterility and Reproduction, (6) Infections, (7) Benign and (8) Malignant Neoplasms, (9) Operative Technique, and (10) Pre- and Postoperative care. The sections on sterility and on malignancy are particularly inclusive and present valuable material concerning both diagnosis and therapy. The section on growth and physiology contains seven excellent fundamental papers which should be of great value to both the experienced and the developing gynecologist. The papers on operative technique stress the indications for various types of operations, the results and the reasons for failure rather than primarily the step-by-step procedure. This adds to the value of this portion of the book.

Static material from the first volume has not been included in the current book but all presentations have been brought up to date and several new subjects have been added. The illustrations are clearly reproduced and appear to be adequate in number.

In general this book presents a good review of the current approach to a number of gynecologic problems. Its particular value is that an author both interested in and familiar with each subject has been selected. It should be a valuable reference for the resident, the practicing gynecologist, and for certain general practitioners who are interested in obtaining more than superficial knowledge of the subjects presented.

                                                    J. ROBERT WILLSON.

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⁶Primary Carcinoma of the Vagina. By Robert G. Livingstone, formerly member, Resident Staff, Gynecological Division, Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York City. Pp. 73 with one anatomical illustration and eight statistical tables. Springfield, Ill., 1950, Charles C Thomas.

⁷Progress in Gynecology. By Joe V. Meigs, M.D., Clinical Professor of Gynecology. Harvard Medical School; Chief of Staff of the Vincent Memorial Hospital, and Somers H. Sturgis. M.D., Clinical Associate in Gynecology, Harvard Medical School. Vol. II. Pp. 801 with 214 illustrations. New York, 1950, Grune & Stratton. $9.50.

This edition of **Midwifery**[8] announces in the preface that it is intended entirely to be used in the training of midwives. Being unacquainted with the formal education accorded midwives in England, this reviewer is not able to judge the fitness of the work as a textbook for such use. Since the book is now in its third edition, however, it might be legitimate to assume that its past acceptance speaks for its fitness as a text, and to judge from it contents the training to which midwives are subjected.

Interesting at the start is the amount of "preclinical" material which must be encompassed before undertaking the obstetric aspect of the subject. The book opens with a section on scientific principles which includes divisions on matter and its structure, osmosis, surface tension, the elements of chemistry and energy. There follows a section on general anatomy and physiology (70 pages), a section on pelvic anatomy (45 pages), and then one on reproductive physiology and the physiology of the fetus (60 pages). In the section on pharmacology, it is interesting to note those drugs which the midwife may use and to find that an additional certificate of proficiency with the gas machine is necessary before nitrous oxide may be administered. These women, in other words, have had no "prerequisite courses," and the entire instruction must stem from this text. The book opens with the broad generalization that "Scientists believe that the whole universe consists only of Matter and Energy," and closes with the specific statement, "Circumcision is practiced far more frequently in hot climates than it is elsewhere." Between these two (presumably accurate) declarations, a vast amount of material is covered, all of it conveyed, of necessity, in the simplest possible terms.

One finds, in the purely obstetric sections, that the only position described for delivery is the left lateral Sims position. The midwife is taught to perform vaginal rather than rectal examinations during labor, and to rupture the membranes early in the second stage (specifically not during a pain). Also one finds: "In some clinics blood for a Wassermann reaction is taken as a routine, whereas in others the patient is only subjected to this inconvenience provided that there is some suspicion of syphilis." And: "Tears of the perineum are extremely frequent—being more common in primigravidae than in multigravidae." And that the midwife is taught to introduce sterile glycerine into the uterus in the therapy of puerperal sepsis.

Presumably this book fulfills its avowed purpose in a satisfactory manner. One would be inclined to doubt, however, that it would have an extensive application in this country.   ALLAN C. BARNES.

The appearance of a new edition of **Williams Obstetrics**[9] is always an event of importance to the specialists in this field of medicine. When, as it must, the editorship passes to new hands, the incidents is one of some real significance in the history of American obstetrics.

The present work, revised and to a large extent rewritten by Nicholson J. Eastman, Professor of Obstetrics at Johns Hopkins University, is the tenth edition. The reader looks with interest at the all too brief historical note printed opposite the title page. The first six (editions) were written by the late J. Whitridge Williams, Professor of Obstetrics in Johns Hopkins University from 1896 to 1931; the seventh, eighth, and ninth were prepared by the late Henry J. Stander, Professor of Obstetrics and Gynecology in Cornell University from 1931 to 1948. The terse statement covers the life story of a work which in its entirety is an epitome of the evolution of American obstetrics in the first half of the century.

[8] **Midwifery.** By R. Christie Brown, Obstetric Surgeon, City of London Maternity Hospital; Barton Gilbert, Obstetrician and Gynecologist, East Ham Memorial Hospital; and Richard H. Dobbs, Assistant Physician, Children's Department, London Hospital. Third edition, 894 pages, 219 illustrations. Baltimore, 1950, The Williams & Wilkins Company.
[9] **Williams Obstetrics.** By Nicholson J. Eastman, Professor of Obstetrics, Johns Hopkins University. Tenth edition. Pp. 1176, with 659 illustrations. New York, 1950, Appleton-Century-Crofts Company, Inc. $12.50.

The new edition represents an extensive revision in method of presentation, in point of view, and in subject matter. Over half of the text and nearly one-third of the illustrations are new. Much additional material, based on the advances of the last ten years, has been added and as a result some of the older material, chiefly now of historical interest, has had to be discarded. The present work is indeed shorter than the ninth edition although by somewhat less than a hundred pages, and has also somewhat fewer illustrations. This slight abbreviation seems a gain, for a book now in its fifth decade clearly must have carried with it many facts and concepts, dear to its editors and readers, which must necessarily, though regretfully, be discarded.

The introduction to the subject of obstetrics in the first chapter represents a departure from the usual. The ninth edition began with anatomy and indeed the external generative organs. Other works on obstetrics begin with the ovum. Dr. Eastman commences with "Obstetrics in Broad Perspective," and deals with birth rates, maternal and neonatal mortality, and with the relation of obstetrics to other branches of medicine. It is an effort to give the student philosophy and orientation, to present needs and social objecives, before he undertakes the detailed study of the care of the individual obstetric patient. This chapter will, one may predict, grow longer in the future.

A number of chapters, which the author lists in his preface, have been completely rewritten. One of the most striking is that on toxemia of pregnancy, of considerable length but embodying most of what is now known about this disorder. Other entirely new sections include those on the ovarian and placental hormones, placental physiology, the estimation of pelvic size and shape, the forces concerned in labor, analgesia and anesthesia and a number of others, in fields which have changed rapidly in the last decade. A special section on hemolytic disease of the newborn, written by Milton J. Sacks, contributes a valuable, if technical, summary of the obstetrical problems relative to the Rh factor.

Williams Obstetrics has in the past succeeded in combining the functions of a reference book to the teacher and practitioner, and that of a textbook, providing stimulus to the student willing to put a little extra effort into his first study of the subject. The present edition promises still to fulfill these two functions. How long a single set of covers will bear the strain of the rapidly expanding knowledge of this subject is uncertain. Perhaps there is still a little room to be gained by eliminations in the future. At any rate the tenth edition will be read both by those who have in the past depended upon this book for constant guidance in their work and also by those who wish a source from which to learn relatively quickly of new discoveries and new points of view.

The new editor is to be congratulated and the hope expressed that he will have the strength over the years to let us have his full quota of new editions.

HOWARD C. TAYLOR, JR.

This book[10] edited by Edmond J. Farris, with chapters by each of fifteen contributors, supplies information greatly needed by those interested in laboratory animals. The procurement of satisfactory experiment animals for laboratory work is a precarious undertaking. This book encourages those needing such animals to raise them and state, "a research worker or technician may undertake the task of breeding and caring for laboratory animals with assurance of some success." However, each chapter is stated to be written by an expert and it cannot be expected that the experience of an expert can be transmitted entirely by written form. It is questionable just how well the information given can result in success in the breeding and care of laboratory animals.

[10]**The Care and Breeding of Laboratory Animals.** By Edmond J. Farris, Executive Director and Associate Member, The Wistar Institute of Anatomy and Biology, E. Van Wagener, Paul B. Sawin, Alden B. Dawson, Leonall C. Strong, Leon F. Whitney, Herman L. Ibsen, F. B. Hutt, Clifford H. Pope, R. C. Hutchinson, Myron Gordon, T. Hume Bissonette, Samuel M. Poiley, Warren P. Spencer, and W. E. Dove. Pp. 515, with 174 illustrations. 1950, New York, John Wiley & Sons, Inc., London. Chapman & Hall, Ltd. $8.00.

The choice of animals covered is wide, and includes monkey, rat, mouse, guinea pig, hamster, rabbit, dog, cat, ferret, opossum, chicken, reptile, amphibia, fish, Drosophila, with a chapter on the control of laboratory pests and parasites of laboratory animals. Most of the chapters have remarks on diseases; the remarks are scant and incomplete. However, this is a subject almost all its own for each species and would require a great amount of space.

The chapter on the hamster is particularly needed with the great interest this animal has created as an experiment animal. An excellent bibliography is given, much of which may not be available to the average worker. The bibliography shows the wide adaptability of this animal to laboratory use and experimentation. The part on laboratory uses calls attention to the limitations of the hamster, many of which are not yet known, but there is ample warning to be careful. Attention is called to caries, since it has been shown that hamsters develop carious lesions in the teeth.

Drosophila are included because of the advantages of such flies in studies of genetics.

Chickens have become an excellent laboratory animal because of the ease with which they are housed and handled, and with the use of the developing chick embryo in all sorts of laboratory work. The chapter on the chicken is excellent, comprehensive, and quite timely.

The chapters on guinea pigs and rabbits are very good. The illustrations are rather poorly reproduced in most cases.

Laboratory workers will welcome this book as a very needed addition to the information for the conduct of laboratory work and investigations. It will, however, be difficult to place this book in the hands of technicians or caretakers, and expect entirely satisfactory results. The supervision of the care and breeding of laboratory animals by someone with considerable experience will be necessary, if this book is to be used with the success that it promises.   EVAN L. STUBBS.

The story[11] of Semmelweis' discovery of the prophylaxis of childbed fever is a familiar one. In the fourth decade of the Nineteenth Century fate set up in Vienna a full-size experiment for anyone who had eyes to see and a brain to think independently. The experiment really began when the minister of education dismissed Lucas Boër for political reasons and appointed Klein as professor of midwifery. Boër, who had been trained under William Smellie, and had introduced English methods in Vienna, had a maternal mortality of 1.3 per cent for a period of more than twenty years. Under Klein the mortality immediately rose to 7.8 per cent. In 1840 Klein set aside the first clinic for the instruction of medical students and the second clinic for midwives. The only difference between the two clinics was that in the first clinic the patients were examined by medical students, frequently fresh from the autopsy table, and in the second clinic the patients were examined by midwives. The first clinic had a mortality from childbed fever four times that of the second clinic. Semmelweis, who was assistant, tried to fit every known theory of the cause of childbed fever into the peculiar situation but none satisfied his inquiring mind. Finally, the death of his friend Kolletschka gave him the clue. Kolletschka died of blood poisoning from a wound received when doing an autopsy. Semmelweis recognized the similarity of the necropsy findings within those he had been seeing in mothers who had died of puerperal fever. Acting on the assumption that he and his students had been carrying cadaveric particles from the dead house to the patients, he gave orders that no vaginal examinations should be made unless the examiner scrubbed his hands in chlorine water until all odor of the cadaver had disappeared. There was an immediate drop in maternal mortality. Later, when a patient with a cancerous ulcer of the cervix was admitted to the ward and childbed fever again became prevalent, he realized that organic particles from the living as well as the dead could cause the disease.

[11]Immortal Magyar. Semmelweis, Conqueror of Childbed Fever. By Frank G. Slaughter, M.D. Pp. 211 with 5 illustrations. New York, 1950, Henry Schuman, Inc., Publishers. $3.50.

This was just the beginning of Semmelweis' troubles. Professor Klein had just published a monograph in which he had proved, to his own satisfaction at least, the non-contagiousness of puerperal fever. Like so many political doctors he brooked no opposition on the part of his subordinates and Semmelweis soon lost his position. Without even telling his friends goodbye, Semmelweis returned to his native Budapest. Here he again conquered childbed fever in spite of bureaucratic opposition. Here he also wrote his great work on the etiology, nature, and prophylaxis of childbed fever and conducted a controversial correspondence with the professors of obstetrics all over Europe. He became mentally unbalanced and died in a mental hospital in Vienna.

Dr. Frank G. Slaughter, a retired surgeon turned novelist, tells this obstetrical story well. He gives an interesting picture of the background for the story. I had not realized until I read this book how much socialized medicine interfered with practice at this time. Skoda, Boër and Semmelweis all lost their positions at the Allgemeines Krankenhaus because their teaching did not agree with the ideas of the minister of education or his minions.   M. Pierce Rucker.

Radiation Therapy in the Management of Cancer of the Uterine Cervix[12] is a practical book of small size presented in composition and style easily read. The subject of cervical cancer is reviewed with thoroughness that suggests the aims of a well-organized tumor clinic—diagnosis, treatment, follow-up, and teaching. Data of fundamental interest are included, but at no point does the work deviate from its strong clinical intent.

The author has drawn extensively upon world literature, with considerable emphasis upon contributions from abroad. Techniques producing the best clinical results are found to have their basis in the Stockholm, Paris, and Manchester methods of irradiation. Utilization of those principles with attention to detail is presented as a means for individualizing treatment by varying sequence, dose, applicators, and the combination of intracavitary radium with external irradiation. For varying a basic technique to meet requirements of tumor response and complications, the author emphasizes the importance of clinical experience as shown in a quotation given from Heyman. "Further, it [improvement in results] cannot depend on an alteration of the routine method of brachy radium treatment. At the Radiumhemmet the Stockholm method is still used; it has been modified only slightly since its adoption in 1914. Finally, there is no difference in the use of additional roentgen ray and teleradium irradiation sufficiently pronounced to explain the improvement. There is, as far as I can see, only one acceptable interpretation; the improved results are due to a superior judgment in handling the individual case, which, in turn, originates from an increased experience."

The author has drawn upon his own clinical experience to present a rationalization of treatment understandable to the student and of value to the seasoned therapist. The reader will be rewarded by an increase in rate of long-term survival and decrease in incidence of complication and failure. If any discordant note be injected it is disappointment that so excellent a book fails to include discussion of interstitial irradiation.

A. N. Arneson.

The third volume of the three constituting the **Atlas of Mahfouz's Obstetric and Gynaecological Museum**[13] bears out in all respects the promise of its two predecessors. The latter were both reviewed in this Journal.

Volume III contains the four concluding chapters, XIX to XXII, which deal with endometrioma, adenomyoma, malignant tumors of the uterus, ovarian cysts (benign and

[12]**Radiation Therapy in the Management of Cancer of the Uterine Cervix.** By Simeon T. Cantril M.D., Director, Tumor Institute of the Swedish Hospital, Seattle, Wash. Pp. 200 with 86 illustrations. Springfield, Ill., 1950. Charles C Thomas. $5.00.

[13]**Atlas of Mahfouz's Obstetric and Gynaecological Museum.** By Naguib Pacha Mahfouz, M.Ch., F.R.C.O.G. (Hon.), F.R.C.P.Lond., F.R.C.S.Eng. (Hon.), Consultant Obstetric and Gynaecological Surgeon, Kasr-el-Ainy Hospital; Consulting Surgeon, Kitchener's Memorial Hospital, Director of the Gynaecological Department of the Coptic Hospital. Vol. III, Chapters XIX-XXII. Altringham, England, 1950, John Sherratt and Son.

malignant), and fetal malformations of obstetrical importance. Of the 250 figures, the last six illustrate specimens described as miscellaneous. These latter are so unique as to merit special mention. The first of these concerned a woman manifesting signs of hydrophobia in the eighth month of pregnancy, although she was bitten by a rabid dog shortly before she became pregnant. No immediate symptoms had developed and no antirabies treatment was given. The baby was delivered by cesarean section and died twenty days later. The patient succumbed to the rabies and the specimen removed post mortem was beautifully illustrated.

Another figure shows a pseudomucinous cyst, a myxomatous cyst attached to the lower pole of the vermiform appendix firmly adherent to it; still another, a large multi-locular cyst filling the pelvic cavity attached to the omentum, the ovaries being entirely free. A fourth figure shows a huge round-celled sarcoma of the omentum in a young woman who suffered from ascites, the tumor extending downward and filling the pelvic cavity. At laparotomy there was found to be no relation between the tumor and the pelvic organs. The last of these miscellaneous specimens was that of a ruptured aortic aneurism which caused sudden death in a woman in the eighth month of pregnancy. Four rare cases of cyclopia are also illustrated.

These are a few examples of the extraordinary material described by Naguib Pacha Mahfouz in the Third Volume of his Atlas. A similar collection to that presented by the three volumes has—to the reviewer's knowledge—never been presented hitherto. It makes· a distinct, original, and valuable contribution to obstetric and gynecological pathology which should be in every medical library and that of the gynecological and obstetric specialist. The illustrations have an exceptionally vivid quality which reflect the specimens of Mahfouz's Museum in a truly mirrorlike fashion.   I. C. RUBIN.

The observations of the authors while using high voltage x-rays in the neighborhood of 800 kv. to treat malignancies of all parts of the body are related. The first of the eleven chapters of this book[14] reviews the physical considerations of x-rays generated by a General Electric KXC—2 installation, of which there were two in this country. As the authors mention, these installations have been made obsolete by more compact apparatus, capable of delivering much higher voltage.

Chapters VII, VIII, and IX are of particular interest to the gynecologist as they pertain to the authors' experience in treating carcinoma of the bladder, breast, and cervix. In the chapter devoted to the treatment of cervix cancer, the authors review the radium techniques as used at the Institut du Radium and Holt Radium Institute, which form the bases for their own radium therapy utilized in conjunction with external irradiation. The tumor dose is calculated, complications are discussed, and end results tabulated. The views expressed relative to the order in which to apply x-ray therapy in Stage I carcinomas are open to debate. The authors' pessimism relative to the effect of irradiation on lymph nodes invaded by disease is unfounded.   HERBERT E. SCHMITZ.

[14]**Supervoltage Roentgentherapy.** By Franz Buschke. M.D., Simeon T. Cantril, M.D., and Herbert M. Parker, M.Sc. Tumor Institute of the Swedish Hospital. Seattle, Wash. Pp. 375. 250 illustrations, 20 color plates, and 19 tables. Springfield, Ill., 1950. Charles C Thomas. $10.50.

Item

American Board of Obstetrics and Gynecology

The next scheduled examinations (Part II), oral and pathological, for all candidates will be held at The Waldorf-Astoria Hotel, New York City, by the entire Board from Thursday, May 10, through Thursday, May 16, 1951. Formal notice of the exact .time of each candidate's examination will be sent him several weeks in advance of the examination dates.

Applications are now being received for the 1952 examinations. Application forms and Bulletins are sent upon request made to:

PAUL TITUS, M.D., Secretary
American Board of Obstetrics and Gynecology
1015 Highland Building
Pittsburgh 6, Pa.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

American Gynecological Society. (1876) *President*, Frederick C. Irving. *Secretary*, Norman F. Miller, 1313 East Ann St., Ann Arbor, Mich. Annual meeting, May 7, 8, 9, 1951, New York City.

American Association of Obtetricians, Gynecologists and Abdominal Surgeons. (1888) *President*, James K. Quigley, Rochester, N. Y. *Secretary*, William F. Mengert, 2211 Oak Lawn Ave., Dallas 4, Texas. Annual meeting Hot Springs, Va., September 6, 7, and 8, 1951.

Central Association of Obstetricians and Gynecologists. (1929) *President*, Russell J. Moe, Duluth, Minn. *Secretary-Treasurer*, Harold L. Gainey, 116 S. Michigan Ave., Chicago 3, Ill. Annual meeting to be held in September, 1951.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President*, Lester A. Wilson, Charleston, S. C. *Secretary-Treasurer*, John C. Burwell, Jr., 416 Jefferson Bldg., Greensboro, N. C.

A. M. A. Section on Obstetrics and Gynecology. *Chairman*, James R. Blos, Huntington, W. Va. *Secretary*, A. B. Hunt, Mayo Clinic, Rochester, Minn. Annual meeting June 11-15, 1951, Atlantic City, N. J.

New York Obstetrical Society. (1863) *President*, Howard C. Taylor, Jr. *Secretary*, Charles M. McLane, 960 Park Ave., New York 28, N. Y. Second Tuesday, from October to May.

Obstetrical Society of Philadelphia. (1868) *President*, James P. Lewis. *Secretary*, George A. Hahn, 255 S. 17th St., Philadelphia, Pa. First Thursday, from October to May.

Chicago Gynecological Society. (1878) *President*, John I. Brewer. *Secretary*, Edward M. Dorr, 30 N. Michigan Ave., Chicago 2, Ill. Third Friday, from October to June, Hotel Knickerbocker.

Brooklyn Gynecological Society. (1890) *President*, Martin Shir. *Secretary*, J. Edward Hall, 429 Clinton Avenue, Brooklyn 5, N. Y. Third Wednesday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.

Baltimore Obstetrical and Gynecological Society. (1929) *President*, Houston S. Everett. *Secretary-Treasurer*, W. Drummond Eaton, 11 E. Chase St., Baltimore 2, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.

Cincinnati Obstetrical Society. (1876) *President*, Edward Friedman. *Secretary*, Robert R. Pierce, 116 William Howard Taft Road, Cincinnati 19, Ohio. Third Thursday of each month.

Louisville Obstetrical and Gynecological Society. *President*, Rudy F. Vogt. *Secretary-Treasurer*, Glenn W. Bryant, Louisville, Ky. Meetings fourth Monday of each month from September to May, Brown Hotel.

Portland Society of Obstetrics and Gynecology. *President*, William Sharkey. *Secretary-Treasurer*, Jack W. Dowsett, 1020 S. W. Taylor St., Portland 5, Ore. Meetings last Wednesday of each month.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President*, Eugene A. Conti. *Secretary-Treasurer*, David Katz, 103 Century Bldg., Pittsburgh 22, Pa. Meetings, first Monday of each month, October to May.

Obstetrical Society of Boston. (1861) *President*, Roy J. Heffernan. *Secretary*, Francis Rouillard, 1180 Beacon Street, Brookline, Mass. Third Tuesday, October to April, Harvard Club.

New England Obstetrical and Gynecological Society. (1929) *President*, Arthur E. G. Edgelow, Springfield, Mass. *Recorder*, Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Mass. Meetings held in May and December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President*, Philip H. Arnot. *Secretary-Treasurer*, R. Glenn Craig, 490 Post St., San Francisco, Calif.

Washington Gynecological Society. (1933) *President*, J. Bay Jacobs. *Secretary*, Allan E. King, 915 19 Street, N.W., Washington, D. C. Fourth Saturday, October, November, January, March, May.

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*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the Society's name is the year of founding.

New Orleans Obstetrical and Gynecological Society. (1924) *President,* John Herring. *Secretary,* E. W. Nelson, 1407 S. Carrollton Ave., New Orleans, La. Meetings held October, November, January, March, and May.

St. Louis Gynecological Society. (1924) *President,* T. K. Brown. *Secretary,* J. Russell Vaughan, 634 North Grand Blvd., St. Louis 3, Mo., Regular meetings second Thursday, October, December, February, and April.

San Francisco Gynecological Society. (1929) *President,* Donald Dallas. *Secretary,* Donald W. de Carle, 2000 Van Ness Ave., San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.

Texas Association of Obstetricians and Gynecologists. (1930) *President,* S. Foster Moore. *Secretary-Treasurer,* Carey Hiett, 603 College Avenue, Fort Worth 4, Texas.

Michigan Society of Obstetricians and Gynecologists. (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President,* O. W. Picard. *Secretary,* Carl F. Shelton, 910 David Broderick Tower, Detroit 26, Mich. Meetings first Tuesday of each month from October to May (inclusive).

Central New York Association of Gynecologists and Obstetricians. (1938) *President,* Nathan N. Cohen. *Secretary,* Merton C. Hatch, Medical Arts Bldg., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May.

Alabama Association of Obstetricians and Gynecologists. (1940) *President,* M. Y. Dabney. *Secretary,* Buford Word, 929 South Twentieth Street, Birmingham, Ala.

San Antonio Obstetric Society. *President,* I. T. Cutter. *Secretary,* S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.

Seattle Gynecological Society. (1941) *President,* Robert K. Plant. *Secretary-Treasurer,* Gerald F. Thomas, 1427 Medical and Dental Bldg., Seattle 1, Wash. Meetings held on third Wednesday of each month, Washington Athletic Club.

Denver Gynecological and Obstetrical Society. (1942) *President,* Edward L. Harvey. *Secretary-Treasurer,* Jack M. Simmons, Jr., 804 Republic Bldg., Denver 2, Colo. Meetings held first Monday of every month from October to May (inclusive).

Wisconsin Society of Obstetrics and Gynecology. (1940) *President,* J. W. Prentice. *Secretary-Treasurer,* Alice D. Watts, 324 East Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.

San Diego Gynecological Society. (1937) *President,* D. Dalton Deeds. *Secretary,* Jesse A. Rust, Jr., 3115 University Ave., San Diego 4, Calif. Meetings held on the last Friday of each month.

North Dakota Society of Obstetrics and Gynecology. (1938) *President,* W. H. Gilsdorf. Valley City. *Secretary-Treasurer,* C. B. Darner, Fargo, N. D.

Virginia Obstetrical and Gynecological Society. (1936) *President,* John M. Nokes. *Secretary,* Chester D. Bradley, 2914 West Avenue, Newport News, Va. Meetings held in April and October.

Columbus Obstetric-Gynecologic Society. (1944) *President,* Roy Krigbaum. *Secretary,* Zeph J. R. Hollenbeck, 40 South Third St., Columbus, Ohio. Meetings held last Wednesday of each month from September to May.

Naussau Obstetrical Society. (1944) *President,* Robert S. Millen. *Secretary-Treasurer,* Peter La Mariana, Williston Park, L. I., N. Y. Meetings, bimonthly from October to May.

Bronx Gynecological and Obstetrical Society. (1924) *President,* Milton D. Klein. *Secretary.* Alex Charlton, 1749 Grand Concourse, New York 53, N. Y. Meetings, fourth Monday monthly from October to May.

Washington State Obstetrical Society. (1936) *President,* Charles Kimball. *Secretary-Treasurer,* E. Gerald Layton, 805 Medical and Dental Bldg., Seattle 1, Wash. Meetings first Saturday in April and second Saturday in September.

Kansas City Obstetrical and Gynecological Society. (1922) *President,* Richard B. Schutz. *Secretary,* William C. Mixson, 320 W. 47th St., Kansas City, Mo. Meetings, last Thursday, September, November, January, and March; first Thursday, May, University Club.

Los Angeles Obstetrical and Gynecological Society. (1914) *President,* A. M. McCausland. *Secretary-Treasurer,* Gordon Rosenblum, 6333 Wilshire Blvd., Los Angeles 36, Calif.

North Carolina Obstetrical and Gynecological Society. (1932) *President,* Wallace B. Bradford. *Secretary,* Richard B. Dunn. Meetings semiannually.

The Society of Obstetricians and Gynecologists of Canada. (1944) *President,* H. B. Atlee. *Secretary,* K. M. Grant. Annual meeting, June. 1950.

Akron Obstetrical and Gynecological Society. (1946) *President,* Alven M. Weil. *Secretary-Treasurer,* Robert M. DeWitt. Meetings held third Friday of January, April, July, and October, City Club of Akron, Ohio Bldg.

Minnesota Obstetrical and Gynecological Society. *President,* James Swendson. *Secretary-Treasurer,* John A. Haugen, 100 East Franklin, Minneapolis 4, Minn. Meetings held spring and fall.

Miami Obstetrical and Gynecological Society. (1946) *President,* John D. Milton. *Secretary,* Richard F. Stover, 701 duPont Bldg., Miami, Fla. Meetings, second Thursday in January, March, May, and November.

Omaha Obstetrical and Gynecological Society. (1947) *President,* Ralph Luikhart. *Secretary-Treasurer,* Donald C. Vroman, 813 Medical Arts Bldg., Omaha 2, Neb. Meetings held third Wednesday in January, March, May, September, November.

Oklahoma City Obstetrical and Gynecological Society. (1940) *President,* John W. Records. *Secretary-Treasurer,* Henry G. Bennett, Jr., 800 Northeast 13 Street, Oklahoma City 4.

Cleveland Obstetrical and Gynecological Society. (1947) *President,* J. L. Reycraft. *Secretary,* G. Keith Folger, 10515 Carnegie Ave. Meetings on fourth Tuesday of September, November, January, March, and May at University Club, 3813 Euclid Ave., Cleveland 15, Ohio.

New Jersey Obstetrical and Gynecological Society. (1947) *President,* J. Carlisle Brown. *Secretary,* Harold Schwartz, 201 Lyons Ave., Newark 8, N. J. Meetings semiannually.

Honolulu Obstetrical and Gynecological Society. (1947) *President,* Guy C. Milnor. *Secretary,* Rodney T. West, The Clinic, Honolulu 14, T. H. Meetings third Monday of each month, Mabel Smyth Building.

Oregon Society of Obstetricians and Gynecologists. *President,* Gerald Kinzel. *Secretary-Treasurer,* Theodore M. Bischoff, 529 Mayer Bldg., Portland 5, Ore. Meetings held on third Friday of each month from October to May.

National Federation of Obstetric-Gynecologic Societies. (1945) *President,* Ralph E. Campbell. *Secretary,* Woodard D. Beacham, 429 Hutchinson Memorial Bldg., New Orleans 13, La.

Dayton Obstetrical and Gynecological Society. (1937) *President,* C. E. Mumma. *Secretary,* N. J. Thompson, 610 Harries Bldg., Dayton 2, Ohio. Meetings, third Wednesday monthly from September through June at the Van Cleve Hotel.

Dallas-Fort Worth Obstetric and Gynecologic Society. (1948) *President,* Asa A. Newsom. *Secretary,* A. W. Diddle, 2211 Oak Lawn Ave., Dallas 4, Texas. Meetings in spring and fall.

Queens Gynecological Society. (1948) *President,* Frederick Carpenter. *Secretary,* George Schaefer, 112-25 Queens Blvd., Forest Hills, N. Y. Meetings held second Wednesday in February, April, October, and December, at the Queens County Medical Society Bldg.

Mississippi Association of Obstetricians and Gynecologists. (1947) *President,* R. C. O'Ferrall. *Secretary,* William Weiner, Barnett-Madden Bldg., Jackson, Miss. Meetings held semiannually.

Florida Obstetric and Gynecologic Society. (1948) *President,* Robert G. Spicer. *Secretary-Treasurer,* Dorothy D. Brame, 1235 Kuhl Ave., Orlando, Fla. Next annual meeting, April, 1951, at Hollywood, Fla.

South Carolina Obstetrical and Gynecological Society. (1946) *President,* J. Decherd Guess. *Secretary,* Arthur L. Rivers, 231 Calhoun St., Charleston, S. C. Meetings held in spring and fall.

Buffalo Obstetrical and Gynecological Society. (1946) *President,* W. Herbert Burwig. *Secretary,* Clyde L. Randall, 925 Delaware Avenue, Buffalo, N. Y. Meetings held on the first Tuesday of October through May at the Saturn Club.

El Paso Gynecological Society. (1948) *President,* C. C. Boehler. *Secretary-Treasurer,* Robert J. Cardwell, 414 Banner Bldg., El Paso, Texas.

Kentucky Obstetrical and Gynecological Society. (1947) *President,* Clyde Sparks, Ashland, Ky. *Secretary-Treasurer,* J. B. Marshall, Louisville, Ky.

Indianapolis Obstetrical and Gynecological Society. (1947) *President,* Gerald W. Gustafson. *Secretary-Treasurer,* C. O. McCormick, Jr., 621 Hume Mansur Bldg., Indianapolis 4, Ind. Meetings held in January, April, and October.

Houston Obstetrical and Gynecological Society. (1939) *President,* Arthur Faris. *Secretary-Treasurer,* J. T. Armstrong, Hermann Professional Bldg., Houston 5, Texas. Meetings held second Tuesday of each month except July, August, and September.

Iowa Obstetric and Gynecologic Society. *President,* J. H. Randall. *Secretary,* William C. Keettel, Iowa City, Iowa.

Memphis Obstetrical and Gynecological Society. (1950) *President,* Phil C. Schreier. *Secretary,* James H. Smith, 1665 Madison Ave., Memphis 4, Tenn. Meetings, fourth Friday, October to May.

Birmingham Obstetrical and Gynecological Society. (1949) *President,* W. N. Jones. *Secretary,* Herbert H. Thomas, 1005 South Twenty-First St., Birmingham, Ala. Meetings four times yearly.

Mobile Obstetrical and Gynecological Society. (1949) *President,* John C. Hope, Jr. *Secretary,* Virginia E. Webb, 1322 Springhill Ave., Mobile, Ala. Meetings held second Thursday of January, April, July, and October.

Utah Obstetrical and Gynecological Society. (1948) *President,* William M. Nebeker. *Secretary,* Vernal H. Johnson, 2279 Jackson Ave., Ogden, Utah. Meetings held second Thursday of October, December, March, and May, at the University Club, Salt Lake City.

Inter-urban Obstetrical and Gynecological Society. (1949) *President*, D. E. Cannell. *Secretary*, E. R. Duggan, 16 North Goodman St., Rochester 7, N. Y. Next meeting will be held in Toronto, October, 1951.

New Mexico Obstetrical and Gynecological Society. (1947) *President*, Louis McRae. *Secretary-Treasurer*, LeRoy J. Bowers, Lovelace Clinic, Ridgecrest Drive and Gibson Ave., Albuquerque, N. Mex. Meetings held third Thursday in March, June, September, and December.